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A FEW OF THE IMPORTANT CONTRIBUTIONS IN THE PAST TO RENAL PHYSIOLOGY*

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In 1662, Lorenzo Bellini, an Italian anatomist, published the first description of the renal tubules which were for many years called Bellini ducts. Four years later another Italian anatomist, Marcella Malpighi, described the renal corpuscles, which at once became known as the Malpighian bodies. He showed that they were connected with the arteries, and guessed, but could not demonstrate, that they were connected with the tubules. Nearly two centuries elapsed before William Bowman, a 26 year old demonstrator of anatomy in London, proved by beautiful dissections that the Malpighian body is the expanded end—the beginning—of the renal tubule; that the intracapsular space is continuous with the lumen of the tubule. Impressed by the resemblance of the tubules to the acini of digestive glands, he conceived that the cells which compose their walls secrete the waste products of metabolism from blood into their lumina. The glomerular capillaries seemed to him peculiarly suited to permit the escape of water from the blood. From these two impressions he constructed the hypotheses that the urinous constituents of blood are secreted by the tubule cells and washed out of the lumen by a saline stream flowing down from the glomerulus.

Bowman's discovery was at once confirmed by another youngster of his own age and of comparable genius, Carl Ludwig, a German physiologist. He examined the structures with the eyes of a physiologist whose ambition it was to interpret vital phenomena in terms of physics and chemistry. He saw the hydrodynamic possibilities of the arrangement of glomerular capillaries, and boldly stated that this structure must be a filter; that the beginnings of urine formation consist in the separation of a cell-free, protein-free filtrate from the blood as it passes through the glomerular capillaries, in volume sufficient to contain all of the dissolved components of urine; that this filtrate in its passage down the tubule is concentrated by reabsorption from the tubule and issues into the pelvis of the kidney reduced in volume, increased in concentration, fully elaborated urine. The significance of the work of these two young men can scarcely be overestimated. In the space of two years (1842-1844) physiology was supplied with a correct structural representation of the unit of kidney function and with two hypothetical conceptions of processes operative within it. A great part of subsequent experimental study has been influenced by these concepts and the results expressed in their terms.

During the following years, experiments instigated by Ludwig, which showed the relations between changes in rate of urine output on the one hand and changes in

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arterial blood pressure or in ureteral pressure on the other, yielded results which were in harmony with this filtration-reabsorption theory. These, together with the influence of Ludwig, r e s u l t e d in widespread acceptance of Ludwig's ideas. But in the years 1874-1883, work by Heidenhain, a German physiologist of Breslau, upset this view. He found that the diffusible dye, indigo carmine, injected intravenously into rabbits, is rapidly excreted in the urine in high concentration, but is not detectable in the glomerular capsules seen in sections of the kidney, excised while excreting it. Hence he concluded that the indigo carmine is not excreted through the glomerulus. It is a diffusible substance; therefore the glomerulus is not a filter, but a secreting structure with the capacity of selecting what shall pass through it.

He reduced the blood pressure in rabbits by section of the spinal cord to a level which abolished urine elimination. Then, having injected indigo carmine, he excised the kidney, found massive accumulations of dye in the lumina of tubules, concluded that it could have found access to them only through the cells of the tubules, hence these are secreting cells.

He raised glomerular capillary blood pressure, which also increases rate of blood flow, but by partially obstructing the renal vein, which decreases blood flow. He found that rate of urine flow always diminished. From this he argued that rate of blood flow through the glomerular capillaries rather than the blood pressure within them is the prime essential in the production of glomerular urine. It acts, he thought, by altering the state of nutrition of the epithelium which covers those capillaries.

He calculated the volume of filtrate from blood plasma which would be required to contain the amount of urea which a man excretes in a day. The figure arrived at was 70 liters. Of this, according to the filtration theory, some 68 liters must be reabsorbed if the day's output of urine were two liters. He did not believe that a volume of blood sufficient to yield 70 liters of filtrate flows through the kidneys in a day; he regarded such an uneconomical process as his figures indicated as incredible.

These facts and arguments and the skill with which they were presented caused physiologists throughout the world to recant their faith in Ludwig; and for the next thirty years the physiology of the kidney was principally taught in terms of the Bowman-Heidenhain secretory theory.

The literature of that period is a literature of debate. Neither the concept of filtration-reabsorption nor that of secretion could satisfactorily answer the objections of the one against the other. Experiments which compelled belief were lacking.

During the years from 1896 to 1917 a great deal of confusing work was published, but the work of two men stands out above the rest. Starling's classical demonstration of the osmotic pressure of plasma proteins, previously thought, because of the great size of their molecules, to be osmotically inert, was of outstanding importance. He showed that their osmotic pressure amounts to some 30 mm. mercury, that is when plasma is separated from isotonic saline by a membrane impermeable to protein but permeable to water and salt, fluid is drawn in to the plasma with an initial force of 30 mm.; or if the attempt is made to filter plasma through a membrane impermeable to its proteins, a pressure greater than 30 mm. mercury must be applied before any protein-free fluid can separate.

Starling then found that in diuretic dogs urine formation ceases when arterial blood pressure is reduced to about 40 mm.; that when the ureter is obstructed, urine continues to be formed until the ureteral pressure has risen to a level about 40 mm. of mercury below that of the arterial pressure. The coincidence of these two values, and the fact that they approximated so closely to his values of the colloid osmotic pressure of plasma, led him to think that the plasma proteins interposed an obstacle to the formation of urine of the same sort as that which they interpose to filtration through a membrane,—in a word, that a

process of filtration is concerned in urine formation.

Experiments by Bainbridge showed that whereas normal frog's urine is strongly hypotonic to plasma, when the tubules (but not the glomeruli) are poisoned with bichloride of mercury, the urine becomes isotonic. His inference was that the glomerular urine is a filtrate which is rendered hypotonic by reabsorptive processes in the tubule.

The next and probably the most important influence up to this time was the publication in 1917 of a monograph on the secretion of urine, by Arthur Cushny, then the professor of pharmacology at the University of London. When Cushny came into the field, the physiology of the kidney was made up, as he said, of "a wrangle of two great views of its activity." In a wrangle, the man who can talk the most usually comes out on top, even though his position may be insecure. It was Cushny's wish to reduce to a minimum the loose talk and confounded theories then enveloping the kidney, while expanding in some small measure the body of solid fact. With a determination that amounted almost to cruelty to theorists, he relegated their confused papers to the library where they could be allowed to continue to collect dust as was their proper fate, while he sought out and organized a few tangible facts which he thought everyone could and would believe. In a letter to Starling, Cushny wrote, "The growth in the literature on the kidney has been extraordinary since the time when you and I began to work on it, and this increase in bulk has not gone along with an improvement of quality, but rather the reverse. No other organ of the body has suffered so much from poor work as the kidney, and in no other region of physiology does so much base coin pass as legal tender. It was therefore necessary to sift thoroughly this mass of printed matter of over 6,000 pages, and I must confess that my patience has been sorely tried by some papers in which the depth bore no proportion to the length." That monograph seems cumbersome now, because from the beginning the author has to fight his way through a maze of elective theories—apart from laboratory data of the first order there were no facts, not even the central idea of glomerular filtration could be set forth as a demonstrated fact. Consequently Cushny endeavored to prepare the way for the student, lest he become wholly lost in the vapors of contradictory speculation, by setting forth what he aptly called his "Modern Theory."

Accepting the premise that urine formation begins in the glomerulus with ultrafiltration, at the expense of the hydrostatic pressure of the blood, of a filtrate containing all the plasma constituents other than the molecularly gigantic proteins, Cushny sought to preserve simplicity by positing that it was the sole function of the renal tubules to reabsorb from this filtrate a fluid of constant and optimal composition, a perfected Locke's solution or protein-free plasma, in such optimal quantities as are required to maintain the optimal composition of the plasma. What was left behind in the tubules passes on into the bladder as urine. The statement that the tubules reabsorb a fluid of constant and optimal composition has been shown to be an over simplification of what actually occurs, that is tubular reabsorption of each constituent proceeds more or less independently of the reabsorption of other constituents. Certain experiments in the 1920's by Starling and Verney and their collaborators proved quite definitely this Cushny's view to be untenable, and Rehberg submitted a great number of theoretical and experimental arguments against it.

Rehberg has especially studied the matter by means of his creatinin-method and has been able to demonstrate, in no indecisive manner, the occurrence of such variations in the composition of the resorbate, and the same result is also evident from certain investigations by Poulsson. Nevertheless, one thinks that Cushny would have been happy to have had each valuable constituent of the glomerular filtrate reabsorbed independently were it not that this explanation seemed to entail a terrifying

multiplicity of operations on the part of the tubule cells, and this multiplicity of function was just what Cushny was determined to expel from renal physiology. Multiplicity of function was apt to be interpreted as vitalism, wherein every cell operates in mysterious ways and under its own wilful determination to achieve some far-off, if not divine, event. Vitalism was still a living issue in Cushny's day, it had scarcely been expelled from nerve-muscle physiology, while many explanations of renal activity were essentially vitalistic in nature. Cushny had no desire to aid and abet this enemy of deterministic science. As he says of his monograph, "If it serves as an advance post from which others may issue against the remaining ramparts of vitalism its purpose will be attained."

Gosta Ekehorn compares Cushny's work with Swedenborg's investigations of the brain, both being instances of how the intuition of genius may be able to bridge over the defects of rather unsatisfactory evidence, so as to construe a general conception, particulars of which may be incorrect, whereas as a whole it may be verified.

Thus, some thirty years ago, physiology found itself in possession of hypothetical concepts of renal function, of an enormous mass of experimentally acquired information bearing upon these, but still unable, with decisive certainty, to answer some of the simplest, most direct questions which had been confronting her from the moment when the true relationship between glomerulus and tubule was discovered.

It was in this milieu of the Cushny renal renaissance that A. N. Richards came home from the war in December 1918. For many years before the war he had been interested in perfusion of the heart and liver, attempting to answer many circulatory and hepatic problems. In 1910 he moved to Pennsylvania as professor of pharmacology where he extended his infusion experiments to the brain and kidneys, with the help of Cecil K. Drinker.

Oscar H. Plant came to Richards' laboratory and together they completed a series of experiments in which they showed that urine formation was related primarily to the blood pressure in, rather than the blood flow through, the kidney, thus offering a rebuttal to an argument that stemmed from Heidenhain, who had found that the rate of excretion of certain dyes is roughly proportional to the blood flow, and generally independent of the blood pressure. More noteworthy, however, was their observation that adrenalin in proper doses caused the kidney to swell, even though at the same time it caused a rise in the perfusion pressure required to maintain a constant blood flow.

This paradox was difficult to explain in conventional terms of vasomotor action, which required vasodilatation, and therefore, a decrease in perfusion pressure, as the basis for the expansion of an organ; but Richards and Plant soon resolved the difficulty by suggesting that the locus of action of the adrenalin was the efferent glomerular arterioles, constriction of which would cause swelling of the glomeruli and anterior portions of the vascular bed at the same time that it caused an increase in perfusion resistance, and therefore in overall perfusion pressure.

Then in 1917 came the war, and these experiments, except for a preliminary note, went unpublished for five years. Richards went to England as consultant to the British Medical Research Committee. In 1917-18 his investigations were confined to the study of histamine and its relation to traumatic shock. In the interval before he went across the Channel to take charge of the Physiological Laboratory of the Chemical Warfare Service at Chaumont in 1918, he also met Arthur Cushny, and the two became close friends.

Upon returning to the United States, he and Plant wrote up their experiments on the perfused kidney, guided by Cushny's analysis of the evidence on renal theory. Then in the spring of 1920 Richards was invited to give a Harvey Lecture and immediately thereafter he came down with an acute appendix. In the ensuing forced vacation he pored over his perfusion experiments and the adrenalin paradox, some

reprints of Krogh's papers on capillaries, and Cushny's monograph. Filled with admiration for Krogh's technic of direct observation of the capillaries in the tongue, foot and mesentery of the frog, he conceived that if he could see the glomeruli at work he might obtain a confirmation of the Richards-Plant adrenalin paradox, and thus in his Harvey Lecture be able to present a demonstrated fact rather than an hypothesis. When he got back to the laboratory in the early autumn he suggested the experiment to Carl F. Schmidt, then an instructor in his department.

It was not long until Richards and Schmidt were seeing under the microscope something no one had ever seen before. On the ventral surface of the kidney an occasional glomerulus could be discerned, the capsule distended with fluid, the blood cells moving in a thick stream through the active capillary loops. The most cursory examination showed that the circulation in some glomeruli was much more active than the circulation in others; and in any one glomerulus capillaries could be seen to change from a state of activity to one of inactivity. Thus Richards and Schmidt came to speak of the "intermittency" of glomerular activity and concluded that in the normal kidney not all glomeruli are active at any one time. This has not been proved to be true in man.

These studies aroused a great deal of excitement in the medical research field. Homer Smith writes, "It was all pretty exciting stuff. I can remember hearing about it in Boston, where I had just come to Walter Cannon's department as a National Research Council Fellow In fact, I heard so much about it in Boston that for a considerable period I labored under the impression that the experiment had been done at Harvard. The basis for this confusion was probably the circumstance that Joseph Wearn, who had been an assistant resident at the Brigham Hospital, went to Philadelphia in 1921 to join Richards as instructor in pharmacology. Wearn probably sent back such glowing reports on the frog kidney, and they were received with such interest, that out on Longwood Avenue the invention seemed to be indigenous." Richards showed Wearn how to look at a frog kidney, asked him to perfect himself in the technic, and to go on looking at it; but to come to him if he had any ideas. Meanwhile, Richards was drifting around and drifted into a meeting of anatomists in which Robert Chambers was demonstrating his microdissecting needle, which he used to manipulate single cells. It occurred to Richards, and he talked it over with Wearn one night, that Chambers' technic might enable them to test their explanation of the adrenalin paradox by applying the drug directly to the afferent and efferent arteriole. Wearn went farther, and suggested that they puncture the glomerular capsule, withdraw the capsular fluid and analyze it. Fired with enthusiasm, they tackled this difficult task and finally succeeded.

The full development of the micro-study of the kidney was a long and arduous affair. Fifteen years elapsed before the definitive publications on the composition of glomerular and tubular urine made their appearance from the Philadelphia laboratories. Arthur Walker joined the staff in 1925, and in later years James Bordley, John Barnwell, R. C. Bradley, Phyllis Bott, and B. B. Westfall.

Now that they were able to see the glomerulus, puncture it with a small capillary, and obtain the glomerular fluid, they were confronted with the problem of analyzing samples of .004 c.c. accurately. In a relatively short time they had developed a capillary microanalytic technic for qualitative determinations. Their results showed that the glomerular fluid obtained from the frog and the Necturus (mud-puppy contains no protein (as a rule); its alkalinity is of the same order as that of blood; it contains chloride, sugar, urea, phosphate, sodium, and potassium, and also some of the dyes which were used in the study of the kidney. The only conclusion that could be drawn from these results is that the glomerular fluid resembles a plasma free filtrate. What was needed was an accurate

quantitative technic to determine whether the glomerular fluid actually is or is not a filtrate. This can readily be appreciated as a task many times more difficult to develop than was the qualitative method.

While quantitative methods were being perfected, other data were being accumulated which were indirectly in agreement with the filtration idea.

H. L. White, of St. Louis, has been interested in renal physiology and has contributed a great deal of experimental work in the field. He suggested and undertook the application of Barber's method for the comparison of the total molecular concentration of glomerular fluid with a plasma-free filtrate from blood collected at the same time. It consists in the introduction of the minute droplet of glomerular fluid into a glass capillary tube, on each side of it is a similar minute droplet of plasma. The tube is sealed and measurements of the length of the three drops of fluid are made during forty-eight hours. If the middle droplet increases in length at the expense of the two adjoining ones of plasma, this means that the original molecular concentration of the glomerular urine was greater than that of the plasma, water passes from the less to the more concentrated fluid. If the middle droplet of glomerular urine decreases in size, it means that its total concentration was less than that of the plasma. More than forty experiments of this sort, made by A. M. Walker, showed them to be approximately the same.

The capacity of a fluid to conduct the electric current depends upon the concentration of ionizable salts which it contains. Hence, if two fluids exhibit the same degree of electric conductivity, this means that the number of ions per unit volume is the same in both. This was shown to be true of the frog's and mud-puppies' glomerular urine and their plasma, by L. E. Bayliss and A. M. Walker.

Finally, Richards et al, found that if suitable precautions were taken, it is possible to make quantitative estimations of the intensity of color of a very minute amount of fluid contained in a glass capillary tube. This knowledge permitted them to find out in what concentration a dye, such as phenolsulfonephthalein or indigo carmine, is eliminated through the glomerulus after it has been injected into the blood; and they could compare this concentration with that which obtained in the blood.

Both of these dyes have been studied. Satisfactory experiments have been made on 21 frogs and in all of these the concentration of dye in the glomerular fluid is the same (within reasonable limits of error of the methods) as that which would be expected if the blood plasma were filtered through a collodion membrane.

Hayman succeeded in measuring the blood pressure in the capillaries of a single glomerulus by an application of the principle of the Riva-Rocci sphygmomanometer. He closed the neck of the tubule; through a capillary pipette in the capsular space raised the pressure within Bowman's capsule to a height at which corpuscles were seen to be flowing through only two or three of the capillary loops instead of all the six which they usually contain, and found that on the average the glomerular capillary mean pressure is 54 per cent of the aortic pressure. The average aortic pressure was found to be 37 cm. of water, so glomerular capillary pressure is about 20 cm. The colloid osmotic pressure of frog's plasma, which is the pressure which must be exceeded before a protein-free fluid can be separated by filtration through the glomerular membrane, is less than 10 cm. These figures demonstrate that the blood pressure in the glomerular capillaries is ample to produce a filtrate.

With time and patience it became possible to adapt to these small quantities of fluid a number of quantitative methods for the determination of individual constituents with highly satisfactory accuracy.

The results show that glomerular urine collected both from frogs and Necturi has the same composition as a plasma ultrafiltrate with respect to total concentration of solutes (vapor pressure), total electrolytes (electrical conductivity), pH, chlorides, inorganic phosphates, glucose, urea,

uric acid, creatinine, phenol red, indigo carmine, and inulin. The last five substances were injected subcutaneously or intravenously before beginning the collection of glomerular urine.

Richards stated, "These results seem to me to leave little room for doubt that, in amphibia, the glomerular urine actually has the composition of a protein-free filtrate from plasma, precisely as Ludwig had imagined 93 years ago. They show that, so far as the frog is concerned, Heidenhain was wrong in denying that indigo carmine escapes from the blood through the glomerular membrane. They give no evidence that the glomerulus possesses any capacity whatever of selecting what substances shall or shall not pass through it if only they are diffusible.

"I call particular attention to the fact that the results with inulin are wholly similar to the rest. This is a polysaccharide of high molecular weight (5100), consisting of some 32 levulose groups probably put together in the form of a chain. Its diffusibility through membranes is much slower than is that of urea, glucose, or sodium chloride, in free diffusion experiments (that is, conducted with no membrane) its mobility corresponds to that of a spherical molecule of 15,000 molecular weight (Bunim and Smith). The fact that this large and slowly moving molecule passes through the glomerular membrane at the same rate as does that of urea, which is only 1/85 as heavy and far more mobile, yields two conclusions: one, that the passages or pores through the membrane are far larger than is necessary for the escape of the normal, diffusible constituents of plasma. The membrane is a relatively wide-meshed sieve. Another, that diffusion plays no significant part in determining the composition of glomerular urine, as I am sure it does in determining that of fluid separated from blood in the systemic capillaries."

Did the evidence permit them to believe that the glomerular process in mammals and in man is one of filtration?

(1) Microscopic study of the glomerulus in the human kidney shows no evidence of the existence of other structures or of more complex cell structures than are to be found in the frog's glomerulus. The epithelium which invests the capillary loops of the glomerulus in man is distinctly less conspicuous than in amphibia. There is no histological evidence of the development of structures which conceivably might serve a more selective process.

(2) The older experiments of Ludwig showed that the mammalian kidney resembles a filter in its response to changes in arterial blood pressure; within limits, urine rate increases and decreases with increase or decrease of blood pressure in the renal artery.

(3) Finally, study of the renal excretion of the polysaccharide, inulin gives evidence which is more than suggestive that mammalian glomerular process is solely one of filtration.

Following the completion of his quantitative studies Richards made the following statement concerning tubular activity, "When we find ourselves forced to believe that for the formation of 1 c.c. of urine per minute more than 100 c.c. of fluid are separated from the blood; that in this separated fluid are contained in twenty-four hours nearly half a pound of glucose, of bicarbonate, and two pounds of salt, little, if any, of which escape into the urine, we are compelled to realize that reabsorption is the chief task which the tubule is normally required to perform."

Visual evidence was long ago obtained of reabsorption both of base and of water. The lumen of a single tubule was distended with a dilute solution of phenol red by intracapsular injection. The tubule was blocked by pressure with a glass rod so that no more fluid could enter the tubule; that within it remained stationary. The colored streak which revealed the lumen gradually changed from a broad, lightly colored band to a narrow thread of concentrated color. Fluid was leaving the lumen, the dye was retained within it. The color remained red until the blocking rod was lifted. Then the column of fluid moved on down the tubule and its color changed abruptly to the

yellow tint, which represents acidity, at the level in the distal tubule at which, we must believe, base is reabsorbed.

Direct evidence of the existence of reabsorptive processes and of the localizations of some has been obtained in the study of the amphibian kidney.

The same methods which were successful in providing fluid from glomerular capsules in frogs and Necturi have also yielded supplies of fluid drawn from different levels of the tubules of these animals. The experiments were far more difficult, however, because of the tortuosity of the tubules and the fact that each is intertwined with its neighbors; because of the narrowness of the lumen, and the necessity of avoiding collection of fluid which had flowed past the point of collecting pipette; because of the necessity also of accurate identification of the site of puncture with reference to the nephron as a whole. A single nephron was identified by injecting dye into Bowman's capsule and watching its passage through the tubule; the deposition of a globule of mercury or oil in the lumen at a point immediately distal to the point of the pipette prevented reflux; a camera lucida scale drawing of the punctured tubule was made by filling its entire lumen with india ink, fixing the kidney, and clearing the part containing it. The puncture hole was easily visible in the cleared preparation, and measurements of the distances to the ends of the segment of tubule in which it occurred were accurately made. Obviously the analytical methods developed in connection with the glomerular problem were equally applicable to fluid from the tubule.

One group of results shows that the glomerular filtrate passes through the entire length of proximal convoluted tubule with little change, either in the total concentration of dissolved substances or in the concentration of chloride. It is only during passage through the lumen of the distal convoluted tubule that the total concentration and the concentration of chloride diminish. From these analyses it is possible to assert that the selective, active reabsorption of NaCl in amphibia is a definite function of the distal and not of the proximal convoluted tubule.

In striking contrast with the behavior of chloride is that of glucose. As soon as the glomerular filtrate has progressed an appreciable distance along the proximal tubule, its glucose content is significantly diminshed. When half-way through, the reabsorption appears to be complete or nearly so. Special experiments in which glucose solutions were perfused through the distal half of the proximal tubule and also through all of the distal tubule showed that the capacity of reabsorbing glucose is possessed by all of the cells of the proximal tubule, but not by any of the cells of the distal tuble (Walker and Hudson).

The reaction of the fluid in the tubule remains essentially the same as that of blood plasma during its progress through the entire proximal tubule (Montgomery and Pierce). At a certain point in the distal tubule it begins to become acid. By injecting indicator solutions (phenol red) into the distal tubule, Montgomery found that the cells which are responsible for the acidification of urine are localized in a region corresponding roughly to the middle third of the distal tubule. There are the best of reasons for believing that reabsorption of base from the tubular fluid is responsible for its acidification.

These reabsorptive processes are abolished when the tubule cells are poisoned as by hydrocyanic acid or mercurous chloride. They are not to be explained by diffusion or by any other familiar physical process. They continue to operate when the fluids within and without the tubule are of identical composition, that is, when no initial diffusion gradients exist.

But there remained the vexing question of tubular secretion: did it actually exist, and if so, what part did it play in the formation of urine?

It might seem that the micro-study technic would quickly answer this question, but the answer was not so easy to attain. Recognizing that highly varying quantities of water are reabsorbed from the glome-

rular filtrate as it passes down the tubules, one cannot say from the degree to which any particular constituent is concentrated over and above the original glomerular filtrate (or, if you wish, the plasma) whether that degree of concentration is due to tubular secretion or merely to the reabsorption of water. Even if tubular secretion is dismissed, one cannot say whether various urinary constituents have been in part reabsorbed. What is required in order to answer the question is a standard of reference for water reabsorption, some substance which can be demonstrated to be neither reabsorbed nor secreted by the tubules; then from the degree of concentration of this standard of reference one can determine the extent of reabsorption of water, and hence whether any other substance has been reabsorbed or secreted. But before that standard of reference was to come, the question of tubular secretion was destined to be answered in the affirmative by E. K. Marshall, Jr.

Trained as a chemist before he went into medicine at Hopkins, Marshall's development of the urease method in 1912 had led him, in collaboration with D. M. Davis, to make observation on the distribution of urea throughout various organs in the body. One day Marshall and Davis happened upon two dogs which had been adrenalectomized by Samuel Crowe, and discovered the marked retention of urea which follows adrenalectomy. This led them into a study of the influence of the adrenals on the kidneys and, prior to the War, in collaboration with A. C. Kolls, Marshall had started a series of experiments designed the influence of the nerves on renal function, experiments which were set aside when he took up work on war gases in New Haven in the summer of 1917. Here, however, he read Cushny's monograph and came to feel that some of the results which he and Kolls had obtained were incompatible with a simple filtration-reabsorption theory.

The war over, and gas warfare no longer of interest, Marshall returned to Hopkins where with Kolls he published their prewar experiments, with additions, in 1919. By this time Marshall had become intrigued with the ambiguities and mysteries of tubular function, and in 1923 he and J. L. Vickers published a paper entitled "The Mechanism of the Elimination of Phenolsulfonephthalein by the Kidney, a Proof of Secretion by the Convoluted Tubules." This proof consisted of the demonstration that after intravenous injection of phenolsulfonephthalein the dye accumulates in the cortex of the non-secreting kidney at a time when the blood pressure is too low to permit the formation of significant quantities of filtrate; and, second, that the dye is to a great extent absorbed or combined with plasma protein, only a small fraction being filtrable; consequently, the quantity of free and filtrable dye in the plasma is inadequate on any acceptable estimation of the rate of filtration to account for the total quantity excreted in a given time. This was the first actual demonstration of tubular secretion.

These experiments were followed in the next year by a paper by Marshall and Crane, adding new and equally convincing evidence, in the demonstration that as the plasma level of phenol red is raised the rate of excretion ultimately levels off and approaches a constant, maximal value; this result is incompatible with a theory of exclusive filtration, but is explicable in terms of filtration plus tubular secretion, the secretory cells becoming saturated at higher plasma levels. At this same time Mayers adduced equally good evidence for the secretion of uric acid by the chicken kidney; the quantity excreted at a given plasma level being inconceivably greater than could be excreted by filtration alone, under any plausible assumption concerning renal blood flow and filtration rate.

Here, in effect, the matter stayed for several years. Proponents of the Cushny theory remained skeptical of Marshall's phenol red experiments, while the proponents of tubular secretion became skeptical of their opponents' reason. Then in 1926, Marshall, browsing through comparative anatomy, discovered that a number of

fishes had been described which possessed purely tubular kidneys. This fact, of course, immediately evoked Marshall's interest in fish urine.

Work on the aglomerular fishes had been undertaken independently by J. G. Edwards in the Naples' laboratory, and within a short time it was clear that this purely tubular kidney, which does not even possess a significant arterial blood supply but is perfused entirely by venous blood from the renal portal vein and at a pressure which is probably below the osmotic pressure of the plasma proteins, can excrete all the ordinary urinary constituents: water, creatine, urea, uric acid, magnesium, sulfate, potassium and chloride; and, among foreign substances, iodide, nitrate, thiosulfate, sulfocyanide, indigo-carmine, neutral red and phenol red. About the only three important things it would not excrete were ferrocyanide, protein and glucose. Marshall recalls this negative discovery as the high point of his experiences in renal physiology.

So, by 1930, the question of tubular excretion was answered in the affirmative. But, as Richards said, "At last he has found an animal that fits in with his theory!" To prove tubular excretion in an aglomerular fish or the tubular excretion of phenol red in the dog, was only to prove the possibility of tubular excretion in other animals; the demonstration really answered no questions so far as the frog or man was concerned, for conceivably the situation might be different in every species, and certainly it would differ for different substances. Further progress required that a standard of reference by which water reabsorption in the tubules, or to use the corollary of this statement, the rate of glomerular filtration, could be measured.

Actually certain European investigators had already made considerable advancement in this direction, but their work had not gained popular recognition in this country. The most outstanding achievements were those of Rehberg when he developed the creatinine clearance test by which he compared the relative clearance of other substances, namely urea. Other European workers who deserve a great deal of credit are Poulsson, Ekehorn, Starling, and Verney. Ekehorn has been a constant worker and writer in the field of renal physiology for many, many years particularly in the Acta Med. Scandinavica.

Returning to the efforts of this country, we find that workers had been attempting to utilize urea in determining kidney function since the early 1900's, with little or no success. About 1921 Thomas Addis and D. R. Drury demonstrated that the rate of urea excretion divided by the urea content of the blood was fairly constant if the urine flow was maintained at high levels by water diuresis. Addis thought that the administered water increased the excretory capacity for urea by a nervous or humoral mechanism; actually the diuresis itself, by reducing the back-diffusion of urea, appears to be the chief factor in explaining the constancy of the Addis index under these conditions. But the administration of water apart, the constancy of the Addis ratio still had no explanation in renal physiology. One of the chief results of Addis' observations was to force the quantitative mode of thinking into experimental renal physiology in this country.

Van Slyke, working with Austin and Stillman, and later with Moller and McIntosh at the Rockefeller Institute, showed that excretory efficiency of the kidney could be expressed simply as the volume of blood cleared of urea by one minute's excretion. They called this volume of blood the urea clearance. With moderate or abundant diuresis, they found that the kidneys of a normal man excreted on the average the amount of urea contained in 75 c.c. of blood were cleared per minute. If the kidneys were damaged by disease, they cleared less blood of urea per minute; in uremia only 3 or 4 c.c. or less. The urea clearance was found to be a sensitive clinical measure of renal function. Visualizing, as in a measuring cylinder, the volume of blood which represents the clearance makes it possible to use a mental photograph in place of a mathematical formula.

The clearance is calculated as (mg. urea excreted per min.) (mg. urea in 1 c.c. of blood). If 15 mg. of urea, for example, are excreted per minute and the blood urea is 0.2 mg. per c.c., the clearance is 15/0.2= 75 c.c. of blood per minute.

In recent years the word "clearance" has broken loose from the excretion of urea and, taking conceptual wings, has become a generalized notion applicable to all aspects of renal excretion. For example we now say that the clearance rate for sulphate is 10 c.c., for potassium, 20 c.c.; urea 75 c.c.; inulin, 130 c.c.; phenol, 760 c.c.; and diodrast, 120 c.c., without knowing how the kidneys clear the blood of these substances, whether by filtration plus tubular reabsorption, filtration without tubular reabsorption, or filtration plus tubular excretion.

Realizing the need for a substance which could serve as a standard of reference for water reabsorption in the tubules, Smith and Jolliffe and later Shannon attempted to find such a substance, a search which led, after a false start with ferrocyanide and xylose, to the use of inulin. They were able to demonstrate that inulin was filtered by the glomerula and not reabsorbed or secreted by the tubules. Now they had acquired a trustworthy method for measuring the rate at which the glomerular filtrate is formed and delivered into the proximal ends of the tubules. The amount of inulin excreted in the urine in a minute divided by the amount contained in 1 c.c. of plasma (that is, plasma filtrate) gives the volume of filtrate in c.c. per minute. Working at the New York University Medical College, they made many such determinations which show that for adult man under basal condition 120 c.c. per minute is the average rate at which glomerular urine is formed. This value is obtained whether urine is being excreted at the rate of 0.5 c.c. per minute as a result of water deprivation, or 15 c. c. per minute because of excessive water intake, or an intermediate rates.

Other carbohydrates such as mannitol, sorbitol, dulcitol, and sucrose have also been found to be excreted by filtration alone in the normal animal. Phlorizin blocks the reabsorption of glucose and brings the glucose clearance up to the level of the filtration rate. The creatinine clearance in both the normal and phlorizinized dog is identical with the simultaneous inulin clearance, but in normal man (and apes) the former is about 30 per cent higher, indicating that in addition to filtration, some creatinine is cleared from the blood by the tubules, as is the case in many of the lower animals. Phlorizin blocks this tubular excretion and brings the total creatinine clearance down to the level of the filtration.

If, as in the case of creatinine, the clearance of any substance, such as phenol red or diodrast, is greater than the simultaneous inulin or mannitol clearance, it can only be because some of that substance is cleared by the tubules, in addition to that which is cleared through the glomeruli. But there must be a limit even to the process of tubular clearance: we cannot clear any substance from a larger volume of blood than actually perfuses the kidneys. The clearance of diodrast in normal man, calculated as whole blood, is approximately 1200 c.c. per minute—one fourth of the total cardiac output. Obviously, this must be close to the total renal blood flow; that is, the extraction of this compound from the renal blood must be very nearly complete and for practical purposes we may take the diodrast clearance as identical with the renal blood flow.

In 1934 at a meeting of the Society of Experimental Biology and Medicine, Smith and Richards discovered that they were working on the same problems and with the same motives and the same substance—inulin.

In 1935 Shannon, studying phenol red excretion in the dog, showed, in accordance with the surmise of Marshall and Crane, that at high plasma levels the tubules do indeed become "saturated" and excrete the dye at a constant maximal rate. This maximal limitation in tubular excretion has subsequently been demonstrated for diodrast and number of other substances in both

dog and man, and may be considered to be a characteristic feature of tubular activity.

It was also in 1935 that Goldrin, Clark, and Smith pointed out that the phenol red clearance at low plasma levels, where the tubules are not approaching saturation) afforded a close approximation to the renal blood flow. In 1937 Goldring, Chasis and Smith showed that the clearance of diodrast, the tubular excretion of which had been demonstrated by Elsom, Bott and Shiels in Richards' laboratory, afforded a closer and quite satisfactory measure of the renal blood flow; and further that the maximal rate of tubular excretion of diodrast (or diodrast Tm) could be used to characterize the total quantity of functional tubular tissue in the kidneys, independently of the blood flow or filtration rate. In 1938 Shannon, Farber and Troast showed that a similar, limiting maximal rate characterized the reabsorption of glucose by the tubules and, in line with diodrast Tm, they called this term glucose Tm. The application of the methods for the measurement of blood flow and filtration rate together with the saturation methods (diodrast Tm and glucose Tm), opens new avenues of approach to the study of the distribution of blood or glomerular filtrate among the functional units of the kidney.

There are several other aspects of renal physiology, which because of their more recent discovery and because of their tendency to change, do not lend themselves well to historical retrospection.

As an example of this, ammonia formation may be cited. For many years urine ammonia was believed to be derived from urea. Recently, however, it has been shown that the majority of the ammonia is derived from the deamination of glutamine by the action of the tubular cells. A small amount is derived from adenosine by the same process; additional studies are, at present, active on this problem.

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THE VALUE OF THE CYTOLOGIC SMEAR IN THE DIAGNOSIS OF CANCER

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NEW ORLEANS

Within the past few years the medical profession and the various cancer societies have been bombarding the public with the information that cancer can be cured —if diagnosed in the early stages of the disease. The cytologic smear is a new tool through which we hope to make possible the earlier diagnosis of a number of malignancies to which this method is applicable. Let me say at the outset that we who are working with this method have no idea of using it to supplant the biopsy. The positive cytologic smear should, whenever possible, be confirmed by biopsy. Only by doing this can we ever hope to establish the proper role of the smear as a reliable diagnostic procedure.

We, of the medical profession, realize

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that our present modes of treatment for malignancies are effective only when our diagnoses are made in the early stage of the disease. Let me take for example the statistics of Garcia and Schlosser who made a survey of five-year survivals in carcinoma of the cervix treated in one year at Charity Hospital. They found that when the malignancy had reached the second stage before treatment was instituted, the five-year survivals were only 51 per cent. Unfortunately in this series, as in most surveys, we find that the majority of the patients did not present themselves for treatment until the malignancy had reached the second and third stages in which the salvage rates are so very low. Earlier diagnosis of cancer is essential if we are to lower these horrible statistics. *Any* method through which we are enabled to make an earlier diagnosis of cancer deserves our most serious consideration. This we hope to accomplish in some measure by means of the cytologic smear.

The cytologic smear has several limitations as a general diagnostic procedure. First, as its name implies, it is applicable only to those regions of the body which produce material from which a smear can be made. And second, we must make our diagnoses from the characteristics of desquamated cells and groups of cells without actually seeing the invasion of tissue by these malignant cells. On the other hand, the advantages of the method are numerous.

1) First, there is the simplicity of obtaining material. The only equipment needed for the vaginal smear is a slightly curved glass pipette with a rubber bulb, several slides with paper clips at the ends to keep them separated, and a bottle of alcohol-ether fixer.

2) Obtaining the smear is not unpleasant to the patient. Because of this, the method can be used to screen large numbers of patients. For urine and sputum examinations only the fresh or preserved specimen is needed.

3) Hospitalization is not necessary for obtaining the smear.

4) The test is inexpensive to the patient —the cost being no greater than that of the usual laboratory procedures.

5) The staining time is short; however, the examination time is longer than that of the usual biopsy.

6) The smear can be repeated as often as necessary, and is therefore excellent for the follow-up of suspicious cases.

7) The smear is an excellent method for following cases after surgery or radiation.

8) The smear often picks up carcinoma *in situ* before the appearance of symptoms or lesions, and is often positive before any other test is diagnostic.

9) The smear offers no conflict with other well established diagnostic procedures, often complements them.

10) The vaginal smear often gives other information about the patient, such as the endocrine status, and shows the presence of many types of infection.

11) The smear is a reliable test in the hands of trained men—and women!

The vaginal and endocervical smears are at the present time recognized as accurate tests for diagnosis of carcinoma of the uterus and vagina. The original work of Dr. George Papanicolaou has been confirmed by many groups of workers, including Ayre, Meigs, Gates and Warren, Isbell, and many others. The cytologic smear is now a routine procedure in cancer detection clinics all over the country. The following chart shows a series of 5329 cases

VAGINAL SMEARS
RELATIVE ACCURACY OF DIAGNOSIS

	NUMBER OF CASES	PROVED CANCER CASES	PERCENT FALSE POSITIVE	PERCENT FALSE NEGATIVE	TOTAL ERROR
PAPANICOLAOU AND TRAUT	3014	194	0	6	0.3%
MEIGS ET AL	1015	154	2.9	10.3	4.0%
GATES AND WARREN	1300	81	1.3	23	2.5%
TOTALS	5329	429	0.7%	0.8%	1.4%

Figure 1

of Papanicolaou, Meigs, and Gates and Warren, showing a total error of 1.4 per cent. Isbell and his coworkers report in the October 1947 issue of the American Journal of Obstetrics and Gynecology, a series of 1045 in-patients whose preoperative vaginal smears checked against postoperative pathologic tissue diagnoses reveal a total error of 1.5 per cent. The error in all these series is largely due to false negative reports in cases of adenoma malignum which does not exfoliate, and carcinoma *in situ* of the fundus.

My own small series of 114 gynecologic cases compares somewhat with the aforementioned statistics, showing at present a total error of 1.7 per cent. Of these 114 cases, 3 were called positive for carcinoma and 4 suspicious. Of the 3 called positive by smear, the biopsies on 2 were positive and the third is now being studied. One case gave a history suggestive of malignancy, one had only a slightly discolored discharge, and the third was completely asymptomatic. Of the 4 cases called suspicious, 2 were negative on biopsy. The first case was a patient with a chronically diseased bleeding cervix that showed cells with very large nuclei on smear. One of our outstanding gynecologists inserted radium immediately after taking a biopsy, sure in his own mind that the cervical lesion was malignant. You can imagine our amazement and discomfort when the biopsy returned with the diagnosis of chronic cervicitis. The second case considered suspicious was that of a severe atrophic menopause with many atypical degenerating cells. Both of these errors were made in the early phase of this study. The other two suspicious cases were also classed as suspicious by Dr. Papanicolaou and are still under observation.

The idea that malignancies of the lung can be diagnosed by finding exfoliated cancer cells in the sputum is not new. This was first described by Field in 1860. Wandall of Copenhagen, an international authority on cytologic diagnosis of carcinoma from sputum, has been in this country studying the technic of Dr. Papanicolaou.

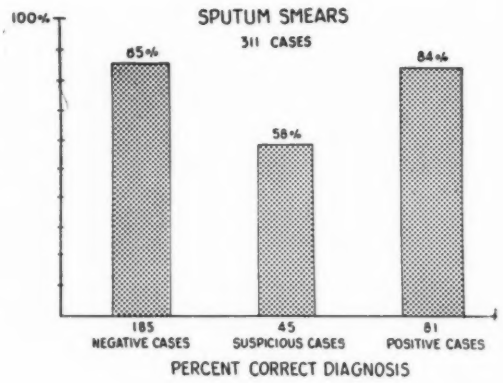
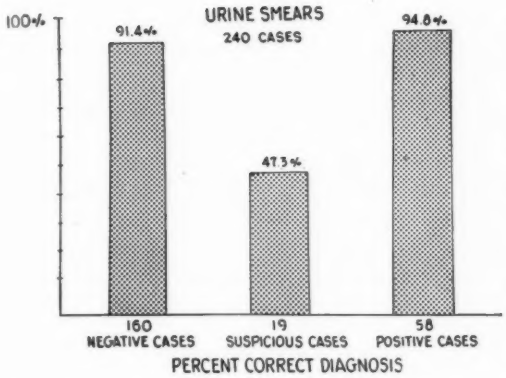


Figure 2

The figures of Wandell and Papanicolaou are in agreement, both having found malignant cells in 84 per cent of cases of cancer of the lung. It is to be hoped that as work progresses in this field positive findings will be even higher. We know that it is possible to obtain positive sputum in some cases before the x-ray shows a lesion. We know too that the cytologic smear is particularly of value in the diagnosis of upper lobe lesions where the bronchoscope can not be used. My own series of cases on sputum is too small to be of any statistical value, but thus far no false positive diagnoses have been made, and, I hope, no false negatives. As to material used, Herbut and Clerf prefer bronchial aspirations, but Dr. Papanicolaou finds that sputum, if correctly obtained and preserved, will reveal just as high a percentage of positive smears.

Diagnosis of malignancies of the genitourinary tract by cytologic smear has been made possible by the technic of Dr. Papanicolaou. We are sometimes able to indicate by smear the probable site of the malignancy, and sometimes we can report only that malignant cells are present. A negative smear of urine is considered at the present time to be 91 per cent correct, and a positive smear 95 per cent correct. The urine presents a technical problem not encountered in working with other smears. There is so little mucus in the sediment that it is difficult to make the sediment stay on the



slide through the staining process. In the East, the technicians coat their slides with a layer of Mayer's albumin before smearing the sediment. I have found Southern urine to be extremely obstinate, and have resorted to mixing the sediment with a small amount of albumin, and thus obtain better results. Catheterized urine is preferable to voided urine as it contains more cells. My own observation is that diagnosis of malignancies of the genito-urinary tract is more difficult than vaginal, sputum, gastric, or exudates, in that there are more pitfalls to be avoided, and single cells are found more often than cell clusters.

Diagnosis of carcinoma of the stomach offers more technical than diagnostic problems. The stomach presents difficulties because of its secretory, digestive, and ingestive functions. Some carcinomas of the stomach are not exfoliative growths, and these will always be missed by smear. The best smears are obtained in cases having achlorhydria. At the present time positive smears have been reported in two-thirds of proven cases of carcinoma of the stomach by two groups of workers.

As to diagnosis of malignancy from ascitic and pleural effusions, no large series has been reported thus far. Dr. N. Chandler Foot, surgical pathologist at Cornell, believes that the cytologic smear will reveal more accurate results than the older method of embedding and sectioning the sediment, as the smear technic causes no slicing or distortion of cells. In my group I have given no false positive reports, but did give a false negative report, knowing when I did that it would be incorrect. This smear was made from a sample of ascitic fluid from a suspected carcinoma of the ovary. The smear showed many RBC and lymphocytes but no malignant cells. The autopsy diagnosis was carcinoma of the ovary with abdominal metastases.

In conclusion, I should like to repeat that the cytologic smear is no substitute or short cut for our older methods of diagnosis. It is a new, accurate, and accepted tool to be used with our other procedures in our ever-continuing fight against cancer.

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ENCEPHALOMYELITIS, EASTERN TYPE, IN LOUISIANA*

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The purpose of this paper is to review what is known of the disease with specific reference to the outbreak that occurred in Louisiana last year.

Equine encephalomyelitis, or sleeping sickness, is an infectious disease caused by a neurotrophic virus and characterized by derangement of consciousness, motor irritation, paralysis, and a high mortality. In the United States two types of virus have been recognized, a highly virulent eastern and a less virulent western type. Natural infection in this country has been observed chiefly in horses, but natural epidemics in humans, pigeons, and pheasants have also been observed.

In 1931, Meyer and his associates isolated the virus during an outbreak that year in California, and in 1933 the virus was isolated during an outbreak in the New England States. These were proven to be immunologically distinct; thus the eastern and western terminology was adopted. Since that time the eastern virus has moved westward and the western virus has spread eastward, resulting in a majority of states having both eastern and western type virus present. Louisiana is one of these states.

The seasonal occurrence of the disease has been from June to November, or the first appearance of frost, thus corresponding with the incriminating data against the blood sucking insects, as it is during this time of year that the insects are more numerous. Mosquitoes have been shown experimentally capable of transmitting the disease and have been found naturally infected with the virus during outbreaks of encephalomyelitis. This was true in last year's outbreak in Louisiana. Dr. Kelser's work revealed that a five to six day interval must elapse before the mosquito is capable of transmitting the disease after having fed on infected blood. It is thought that during this time the virus undergoes maturation or multiplication. The mosquito after becoming infected with the virus remains capable of transmitting the disease all the rest of its life. With this in mind it can readily be understood that winds can easily spread these infected mosquitoes over many miles and in all directions. It has also been shown that the Rocky Mountain spotted fever tick, Dermacentor andersoni, is capable of transmitting the virus through the egg to the offspring, thus probably acting as a reservoir of infection. However, humans, horses, chickenmites, and migratory birds have all been considered possible reservoirs but as yet no definite proof has been found. The course of the disease is from a few hours to a few days. At the height of the outbreak death usually occurs in from two to four days. A few drop dead without showing previous symptoms. The mortality in the western type of the disease is about 40 per cent while that of the eastern type is 90 per cent and higher. In Lou-

*Read before the Sixty-eighth Annual Meeting of the Louisiana State Medical Society, Monroe, April 14, 1948.

isiana last year there was a 98 per cent mortality.

The period of incubation is from one to three weeks. The first or febrile stage of the disease usually goes unnoticed by the owner of the horse, but the temperature may run from 103 to 106° F. It is during this time that the virus is present in the blood stream. The virus then makes its way to the central nervous system and the dominant symptoms of psychic derangement, motor irritation, and paralysis reveal themselves. Mental depression in some form, from dullness in the early stages to complete coma near the end, is an almost constant symptom. Motor irritation is commonly present. Especially noticed are clonic spasms of certain groups of muscles, and involuntary forward or circling movements. Paralysis of the throat is always present, resulting in the accumulation of food and saliva which gives rise to a fetid odor and a nasal discharge. The paralysis finally becomes complete and death ensues.

Upon postmortem there are no gross diagnostic lesions. In the eastern type, histological examination of the brain reveals perivascular lymphocytic infiltration and degeneration of the nerve cells being more pronounced in the cerebral cortex. Similar changes are produced by the western type of the virus, but to a lesser degree of intensity.

A clinical diagnosis of encephalomyelitis can be made on its epizootic nature, seasonal occurrence, and symptoms of derangement of consciousness and paralysis. Botulism, commonly confused with encephalomyelitis, is usually confined to one farm. The symptoms of paralysis are present, but encephelitic symptoms are usually absent.

A differentiation between eastern and western types of encephalomyelitis can be made clinically because the symptoms of the eastern type are more severe than those of the western type. The course is much shorter and there is a higher mortality in the eastern type.

A laboratory differentiation is made by means of animal inoculation, using guinea pigs, mice, or rabbits. Serum protection test, that is inoculation of these animals with serum of specific type followed with injection of fresh brain tissue, also the complement fixation test may be employed for the purpose of determining the type of virus.

Treatment of the sick is entirely symptomatic. Anti-equine encephalomyelitis serum is of doubtful value. If the animal is unsteady but still able to stand, slings or similar support are recommended. Water is given twice daily through a stomach tube, and this may be supplemented with physiological saline 1000 c.c. or dextrose 40 per cent solution, 500 c.c., given intravenously daily. Various drugs and products have been recommended, but have been found to be of little or no value.

Very few animals were treated in Louisiana during the outbreak because of the futility of the treatment. The veterinarians thought it more important to spend all their time vaccinating unaffected animals in order to prevent the spread of the disease.

Following the discovery that the virus could be inactivated by formaldehyde solution without destroying its antigenic properties and that it could be propagated in chicken embryos, a very effective vaccine has been developed. The present day product consists of formalin-inactivated suspension of virus bearing, chick embryo tissue.

For the prophylatic vaccination of horses, the vaccine is administered intradermically in two doses seven days apart.

It might be said that during the height of the outbreak in Louisiana, many horses and mules came down with the disease between the time of the first and second injection. This was probably due to the fact that these animals had the disease in the incubative stage at the time of the initial injection. The immunity resulting from the two injections of vaccine persists for six months to one year. Because both the eastern and western type virus are found in Louisiana, it is necessary to use bivalent vaccine which is a vaccine made from both eastern and western type virus.

In Louisiana last year the disease made its first appearance near Crowley during

the latter part of June. In little more than a month's time it had spread all over the southwestern parishes (fourteen in all) with sporadic cases in surrounding parishes. When the disease disappeared in October, we found that some 5,000 horses and mules had died from the disease and approximately 65,000 animals had been vaccinated.

In hopes of preventing another outbreak this year, the Louisiana Livestock Sanitary Board is recommending that the farmers have their horses and mules vaccinated early, so that the last injection of vaccine is given not later than May. The Board has also recommended that all horses and mules be sprayed every twenty-one days with DDT solution, in order to control the mosquitoes that feed on these animals, and spread the disease.

CHOICE OF METHOD OF TREATMENT OF PSYCHIATRIC PATIENTS*

SAMUEL BARKOFF, M. D.

NEW ORLEANS

Psychiatric treatment aims to help the individual direct his activities so as to achieve increased satisfactions which are appropriate to his environment. This does not mean that ideally the psychiatrist hopes to help his patient conform to all of the demands of his family, his friends and of society but rather to help him to achieve a more comfortable balance, be more able to make his own decisions, and having made them, to be satisfied with them. There are positive forces in the direction of mental health in most persons which involve a continuous integrative process. However, the environmental forces of early life may have badly disturbed the direction and pattern of this integrative process so that the individual continues to exhibit infantile or childhood patterns which are very much out of keeping with adult status. The person who insists on remaining in bed to escape unusual pressure at work is in reality regressing to a form of infantile behavior.

A person may often display a seemingly good adjustment to his environment until some catastrophe or increased responsibility makes a demand he is unable to cope with and he is then compelled as the only possible adjustment available to resort to a more infantile mode of behavior. For example, a fifty year old railroad clerk had to be hospitalized after the death of his mother. He had been a quiet, sedate person, devoted to his mother, who in turn took care of his needs even to the extent of planning his vacations and purchasing all his clothing. He felt helpless without her, became very agitated and repeatedly asked, "What shall I do, what shall I do? Please help me". He was really just like a small frantic child and there was actually a childish whine in his voice.

Involved in the therapeutic process is the necessity for the patient to recognize the nature of his own behavior.

The two brief illustrations given bring out an important point. It is very hard for anyone to accept the fact that he is behaving immaturely. It is quite a blow to one's self-esteem and often very painful. Patients would prefer believing they have physical symptoms to accepting that theirs is a behavior pattern more fitting a small child.

The need for early therapy is of utmost importance for the avoidance of fixations of infantile behavior patterns with their increasing distortion and displacements, and the danger of further regression. These make for a more difficult treatment situation. This is indeed obvious in such disorders as the phobic states where the limitation of activities tends to increase or in the obsessive-compulsive disorders where there are further symptoms which develop as extensions of the earlier symptoms.

Today, the psychiatrist is expected to offer more than just a diagnosis with perhaps a recommendation for sedatives and rest or a demand that the patient give up his foolishness. Too often such a procedure leaves the individual emotionally in exactly the same situation as he was when his re-

*Read at Meeting of the Orleans Parish Medical Society, January 26, 1948.

gression or disintegration began. In the event of prolonged rest, a somewhat better physical condition is achieved and a feeling of new psychic strength arises. The patient now has the energy to bang his head harder than ever against the same psychological brick wall. Therapy must be aimed through the understanding of the dynamics of his illness at helping this person past what appears as an impregnable barrier.

Many problems seem very simple to everyone but the person involved. "Why don't you use your common sense and leave your husband?" is repeatedly asked of the wife of the alcoholic when she seeks advice. Most likely, the real reason why she married him in the first place and why she is compelled to hang on to him will remain a mystery to her. If eventually she can be brought to understand the part played by her masochistic tendencies, her guilt feelings, her identification with her husband and her inferiority feelings she can then permit herself to make suitable decision about her future course. People will use common sense only if they are in the proper psychic situation to do so, and the work of the psychiatrist is to help them reach a position where reason can function.

How do we go about putting the individual in a position to make suitable decisions? Obviously, some persons are so disordered that the possibility of reintegrating is very poor and protective care is of immediate importance for both the community and the person.

The diagnostic interviews are of utmost importance in several ways. First, we learn the patient's concept of the development of his disorganization and the nature of his malfunctioning as he understands it. His behavior and approach to the interviews gives us an idea of his ability to handle situations, his capacity to relate to other persons, the techniques he uses in establishing relationships and lastly an idea of his readiness to accept help. The diagnostic interviews are themselves of therapeutic value in that many patients find it not too difficult to develop new insights if able to talk to someone who in a non-judgmental, non-critical atmosphere can help them. A rapid resumption of healthy functioning often occurs especially when the person is seen at the beginning of his difficulty and before he has begun to mobilize his more infantile approaches.

Many individuals are so afraid to handle new insights that attempts to guide them even slowly are often of no avail. They are so fearful of their own emotional drives, and experience such pangs of guilt that they can only tolerate a therapist who will approve of their mishandling of the situation. Frequently, they are seeking an organic basis for all their troubles and reject any physician who fails to agree with them. The slightest variation in blood pressure, blood count or basal metabolic rate may be pounced on as the cause of every difficulty.

Other persons may show their resistance to therapy quite early in the diagnostic process by finding all kinds of obstacles to treatment. Occasionally their reasons for objecting are valid but more frequently they are not. While some patients raise objections to the fees involved, the time required, the inconvenience of appointment hours, the distance traveled, and so forth, it is amazing how others in more difficult circumstances overcome these obstacles. Frequently, we are faced with those who make impossible demands in regard to time of appointments or fees, those who repeatedly break, forget or arrive late to appointments, and those who demand that the therapist immediately give them the answer to all their problems or quickly remove a disabling symptom. Experience has repeatedly brought out that the psychiatrist will not help his patient if he tries to concede to these unreasonable demands. It is necessary to expose these demands as forms of resistance to therapy before effective treatment is possible.

The management of the patient who rejects therapy is usually difficult when the patient previously has had an authoritative source to support him in his own distorted viewpoints that he is organically ill or that psychotherapy is dangerous. The fact is, of course, that it is extremely rare for a

patient to become worse in the hands of a competent psychotherapist. This may happen when the person is already at the point of complete disintegration or very rapidly headed that way at the time the psychiatrist is consulted. Experience has shown that the very fact that someone has demonstrated an interest in helping another person is nearly always of some value. Many persons who bitterly complain about a previous therapist admit later that actually they profited from the experience.

An evaluation of the degree and type of rigidity of a patient's personality structure is of importance in planning therapy. Some persons are so unapproachable by means of the ordinary therapeutic interview that the psychiatrist must limit his help to recommendations about daily routine, vacations, changes of work or residence, or the use of sedation in periods of stress. When the patient is greatly disturbed or depressed, shock therapy may be indicated and even periods of hospitalization. These are at best, aids or poor substitutes for the intensive interviews as the method of treatment.

As I have already suggested, the interview involves more than just talking. It is typically a combination of two persons working together on one set of problems. Intellect, experience and understanding, emotional maturity, intuitiveness and patience are the factors that play the major roles. The patient is really making use of the therapist's strengths in these qualities to supplement his own.

The therapist's role is far from being a passive one in the interviews. Because of the complexity of his patient's performances, he must do a great deal of listening and observing. In some instances his role may be largely one of encouraging and offering support. At another time the approach may be an inquiring one, perhaps, even to the point of demanding information. When the patient expresses a feeling of being weak and helpless, it may be necessary for the therapist to decide whether to be frustrating or supportive. The therapist needs to be able to evalute whether the patient is capable of handling a given situation and upon this depends his choice of technique at that point. If the therapist feels the patient is able to make the next move it may be necessary to focus attention on the particular problem involved, repeatedly bringing the patient back to the problem when he avoids it.

Psychotherapeutic interviews may be categorized in two main types. In the first, only limited insight is possible, advisable or feasible, and this may be called limited psychotherapy. The second type is psychoanalysis. In limited psychotherapy, the approach may be largely supportive as may occur when the patient is faced with an unhappy or unfortunate situation and needs support to enable him to carry on his daily routine. The principal aim in such situations is largely the avoidance of regression. Again, when time may be a factor, the therapist may make suggestions or approve or encourage a course of behavior. Situations may be discussed without attempts to go too deeply into the past or without too much bringing in the patient-physician relationship on the part of the therapist. There are occasions when the patient insists on doing so, or when it is absolutely necessary to discuss these relationships in order to make possible or to maintain even a limited contact. Limited therapy as described is rarely an adequate substitute for psychoanalysis. Very often, however, it does enable a patient to carry on fairly well but there still remain many conflicts which would be better resolved in the long run. It is true that many persons, after limited therapy, will function better than they did before and feel no further need for treatment. The usual occurrence is that the resolution of the more superficial conflicts allows the more deeply repressed conflicts to come to the surface and this makes further therapy almost a necessity. Although such persons are actually functioning better, they have come to recognize the existence of underlying anxiety, of their poor handling of instinctual drives, their hostilities towards others and their unsatisfactory interpersonal relationships. The persons who manage to stop at this point

usually have some aim such as marriage or a new position that may serve as a new source of satisfaction. In many instances we find that this breaking of the ice offers sufficient satisfactions to some persons and their need for further therapy ceases. Contrary to common belief, limited therapy really requires much more skill and experience than does psychoanalysis. The average course of psychoanalysis is two to three years during which the subject has interviews at least three or four times a week. There is much opportunity for reflection; the material is more carefully studied and the psychoanalyst is confronted with the conflicts in a variety of ways so that he is more certain of the ground he treads. He is more certain of how much interpretation his patient can tolerate, has opportunity to present an interpretation repeatedly and to demonstrate its validity just because the same conflict presents itself repeatedly. The psychoanalyst is able to make better use of the patient-physician relationship and its distortions, better known as the transference, that are an important source of information. He has more opportunity to study his own counter-transferences and keep his own problems out of the treatment situation. He is able carefully to trace or reconstruct the development of current attitudes and modes of behavior. All of this is particularly valuable in chronic neuroses or character disorders where repeated demonstrations of the existence of conflicts are required before they are accepted. Analysis may be likened to digging up weeds in that a conflict may be defended in a number of ways and it is necessary to expose all the defenses or else new ones will develop. Psychoanalysis aims at emotional insight which is much deeper than intellectual insight.

Patients repeatedly state they know why they behave in a certain way but are unable to do anything about it. It is questionable whether such a statement is ever true because in all successful analyses it invariably happens that the patient is compelled to give up his neurotic behavior pattern when he realizes how costly such behavior really is in every way rather than just in a few respects. For example, the Don Juan who has been so proud of his many conquests no longer gets very much satisfaction out of them when he realizes that these are largely a display of a hostile attitude toward his mother and other women, that he needs to prove himself sexually, that he may be a cause of severe emotional disturbance in his sexual partner, and that he himself could not tolerate friendly relationships of a lasting nature.

Considering that psychotherapy is a recently developed field, tremendous strides have been made in technique. Psychiatrists are well aware of the need to shorten treatment time and to make the benefits of therapy available to more people. With an increasing number of well trained psychiatrists and continued research, a great deal more can be expected in the coming years but it is not to be hoped that psychotherapy will ever satisfy the wish for miracles that so many persons understandably entertain.

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PSYCHIATRIC EMERGENCIES*

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NEW ORLEANS

It is my intention to discuss here some of the common psychiatric situations in which prompt and appropriate treatment is imperative for the minimizing of morbidity and mortality. In particular, I wish to consider those conditions that ordinarily fall to the lot of the general practitioner, internist, or surgeon, for care, rather than those emergencies likely to occur in a psychiatric hospital. In considering the emer-

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gency nature of a psychiatric condition we must keep before us the fact that it is not the possibility of a fatal outcome that is ordinarily the danger. The physician is usually aware of that danger and recognizes the need for prompt attention to avoid it. More important perhaps, and I believe more often insufficiently considered, is the danger, often also avoidable, to the patient's future mental and emotional health which may follow upon an acute situation. Since most of the common situations are cared for by physicians other than psychiatrists, a real contribution to mental hygiene can be made by them. This is preventive medicine.

POTENTIAL SUICIDE

When one thinks of a psychiatric emergency, the threat of suicide generally comes first to mind. While this is certainly something requiring special psychiatric handling, usually in a hospital setting, still in most instances it is the family doctor who is called upon by those around the patient when such a threat is believed to exist. The physician then must decide whether the patient is potentially suicidal or not, and if so, must be able to take appropriate action. An adequate discussion of clinical indications of the presence of an active suicidal trend in a patient lies outside the scope of this presentation. However, certain points may be emphasized briefly. Most bona fide suicidal attempts and successful suicides occur either in the course of a severe depression or in catatonic excitement. In the latter condition suicide is likely to be a sudden impulsive affair, a part of the tremendous general expression of aggressive impulses. Attacks on others may occur as well. A sufficiently depressed person kills himself with deliberate and considered purposefulness. Such a decision may be reached rather rapidly and carried out forthwith in which case no opportunity for prevention may appear. More commonly the patient broods over the matter and harbors ideas of self-destruction for a more or less considerable period of time. He may or may not apprise others of what is in his mind. It is not true that a person who talks suicide never does it. Other clinical indications are more important. A serious suicidal intent on the part of the patient may be strongly suspected when the patient is obviously sad and depressed but not too retarded in actions, does not cry, expresses unshakable hopelessness, or speaks of suicidal ideas more or less matter of factly without seeming to be dramatic or to overdo it. Suicidal threats made in a definitely dramatic manner, evidently for effect, particularly on relatives, are apt to be gestures of a hysterical personality. These people often make actual attempts at suicide but are careful not to complete them. A patient who is extremely depressed and retarded may have insufficient drive to carry out his desire for self-destruction, so that suicide is most likely to occur as a patient is going into or coming out of a deep depression. The general physician often sees such patients complaining of various somatic dysfunctions but particularly of profound lack of energy and a feeling of being no longer able to cope with ordinary day to day activities. The general physician's important contribution to the handling of such cases is his early recognition of suicidal potentiality and his securing prompt psychiatric referral and hospitalization. While it is probably true that even in a good hospital an intelligent person bent on suicide may be able to carry it out in spite of the best supervision, certainly the danger can far more readily be coped with than in the patient's home.

INSOMNIA AND RESTLESSNESS

Insomnia and restlessness are common complaints of patients suffering from depression or chronic anxiety and tension. The symptom of insomnia would seem to require sedative and hypnotic drugs for its alleviation, and such drugs do, of course, have an important place in its treatment. The tendency, however, of the physician is to rely too exclusively on these drugs and not to exercise sufficiently close supervision over the amounts taken. The writing of prescriptions which do not contain the "non repetatur" direction will allow repeated refilling, so that the patient may

take the drug regularly long past the period desired. It is wise practice to include that direction on all sedative prescriptions and to order relatively small amounts. Only rarely is the administration of powerful hypnotics necessary for more than a few days at a time. The meaning of the foregoing remarks in regard to emergencies is that drug intoxication with possible serious consequences may develop when the use of these drugs is abused. Symptoms and signs of intoxication may appear insidiously, be at times obscured by the patient's preexistent complaints, and may be unrecognized until a dangerous toxic state has been reached.

This picture is particularly likely to occur in bromide intoxication. The slow excretion of bromides allows a cumulative increase in blood levels so that long contained exhibition of relatively small amounts can result in toxic concentrations being reached. Bromidism may be seen following long use of certain proprietary preparations containing varying quantities of bromides. There is a typically organic type of psychotic reaction characterized by restlessness, marked confusion and disorientation, sometimes hallucinatory phenomena. A rash is often present but not in all cases. Diagnosis may be confirmed by the finding of high levels of bromide in the blood. The estimation of blood bromide concentration is probably indicated in any case of a toxic delirioid reaction having no obvious cause. The specific therapeutic measures, aside from the primary one of stopping further intake of the drug, is the administration of sodium chloride, parenterally and by mouth, to promote excretion of bromide.

More commonly used now than the bromides are the barbiturate sedatives and hypnotics. While the factor of cumulative action is not so important as with the bromides, large dosages of barbiturates are frequently given and may cause serious toxicity. Self-administration also is frequent, at times in large doses with suicidal intent, more commonly for insomnia and other manifestations of anxiety. Barbiturate poisoning may appear as a chronic confusional state with drowsiness and apathy, as an acute delirium, or, when very large doses are taken, as a profound shock-like state with marked depression of the vital centers. In the last named reaction means of supporting and maintaining the function of these centers form the most important part of treatment. The use of a respirator of a positive pressure type (or manual artificial respiration) with 100 per cent oxygen is of prime importance. Picrotoxin is the central stimulant of choice. A vaso-pressor drug will usually be necessary; neosynephrin has been found to afford a more prolonged and evenly maintained increase in blood pressure with less tachycardia than adrenalin. An important point in the treatment of patients habituated to large doses of barbiturates is the inadvisability of sudden and complete withdrawal of the drug. Not only will distressing anxiety sypmtoms result, but not infrequently convulsions may occur when the long-standing cortical depressive influence is suddenly removed. A more gradual decrease in amounts and frequency of dosage with substitution of another barbiturate for the one habitually used will avoid these complications.

DELIRIA

Deliria in the course of severe systemic diseases are not uncommon and require prompt handling both because of the dangers inherent in the delirious state and the deleterious effect on the treatment of the primary condition. General measures indicated in the treatment of any acute delirium regardless of underlying cause may be detailed here. The patient should be subjected to as little in the way of changing environmental stimuli as possible; therefore, a quiet room is advisable, and lighting should not be bright or conducive to shifting shadows which may be frightening. Nurses and attendants should be few and not changed frequently. Fluid intake must be maintained, parenterally if necessary, with added vitamins and tonic doses of insulin. There is in all cases the possible danger of death from exhaustion or at times sudden unexpected death in an acute toxic delirium.

A special, and exceedingly common, cause of toxic states and deliria needing early and adequate treatment is of course alcohol. The danger to life in delirium tremens is sufficiently well attested by the too frequent reports of sudden deaths among alcoholics in jails or elsewhere. Much more common but more important from the viewpoint of prevention are the less severe grades of alcoholic disturbance. These conditions are the precursors of delirium tremens into which they may develop unless properly handled, which almost always can be done. Nearly every physician will at some time be called upon to treat such a situation, and I believe that such care is in the domain of the general physician rather than that of the psychiatrist. In any event psychiatric treatment and especially psychotherapy of such a case must await the control of the toxic condition; nothing can be attempted in the way of treatment of the underlying alcoholism until then. These cases may if necessary be satisfactorily treated in the home although usually treatment in a general hospital may be advisable. The more severe instances of course may have to be sent to a psychiatric unit or hospital. A simple and easily administered detoxifying regime has proved to be very effective in the usual case. In 50 c.c. of 50 per cent glucose is placed 20 units of regular insulin and 100 mg. of thiamin chloride, the whole being given intravenously every four to six hours over a period of one to three days. In the home or in milder cases generally sugar in fruit juice and thiamine orally may be substituted with efficacy. The patient is to be encouraged to eat and ordinarily will begin to do so under the stimulus of these procedures. The complete withdrawal of alcohol is probably neither necessary nor advisable. The patient is more likely to cooperate in treatment if an occasional small drink is provided or if he is given to believe that he may have a drink if he feels an imperative need for it. The mere knowledge that a drink can be had may enable the patient to do without it. Dexedrine (dextro-amphetamine) in 2.5 to 5 mg. doses two or three times in the forenoon may aid in restoration of energy and improvement in mood. In the presence of much restlessness some sedation may be necessary. Chloral hydrate is often quite effective; the judicious use of barbiturates such as seconal is not contraindicated.

ACUTE ANXIETY STATES

I should like to touch briefly upon a group of situations the emergency aspect of which will be less apparent. Every psychiatrist is familiar with acute anxiety states, amounting at times to panic reactions which may be the response to a more or less sudden activation of emotional conflict by internal or external influences. Often enough such a state is the precursor of a severe and acute psychosis of a schizophrenic type, a catatonic excitement. In some instances this serious development may, I believe, be obviated by proper handling of the preliminary reaction. The patient may consult his physician ostensibly because of rather obvious somatic expressions of anxiety; the "jitters," palpitation, giddiness, headache, etc., and may have difficulty telling the doctor about his real fears—of psychosis, of losing the mind, and behind that, often enough, concerns about homosexuality. Not that these patients are overtly homosexual; rather some occurrence, perhaps an actual seductive approach by a homosexual, has mobilized latent conflicts concerning such impulses and aroused in the patient fears of possessing such inclinations. The busy physician may be tempted to pass off the patient's complaints rather lightly and send him away with a prescription for phenobarbital and the admonition to "forget it." Unfortunately he may be able to "forget it" only by becoming psychotic. This eventuality of course many times cannot be prevented even by expert psychiatric attention. But in many instances the general physician may be of real help to such a patient at the cost of only a moderate amount of time and interest. The experience of talking about these carefully hidden fears to a calm and sympathetic listener is therapeutic. The physician may reassure

the patient about the unreality of his worries and point out the normality of his impulses. A little expenditure of time may make the difference between mental health and illness.

SUMMARY

A few of the emergencies of a psychiatric nature which the general physician may often see have been discussed. The importance of early recognition of delirious states, the avoidance of over-use of sedative drugs, and the possibility of preventing psychotic reactions have been stressed.

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DISCUSSION

Dr. C. S. Holbrook (New Orleans): Dr. Johnson has brought us a presentation in which most of the common emergencies we see in psychiatry are brought out. I can only emphasize some of the things he has said. Suicide, of course, is the real danger when the patient is depressed, and if it occurs, the family and the physician will have a feeling of guilt, and possibly justly so. Suicides should be preventable, but in some instances they are not, for the person who intends to commit suicide may outwit everyone who is trying to prevent it, even in well regulated hospitals. That is not as true today as formerly. Today with modern treatment, with use of electroshock treatment, these patients do not have to go through prolonged periods in which they are harboring ideas of suicide. These suicidal intentions can be eliminated in the course of two or three days. If a patient who is suicidal is admitted the thing to do is to give electroshock treatments frequently, an intensive treatment, maybe two treatments a day, or even three a day. In that way within two or three days the danger is over, at least largely so. All definitely suicidal patients should be placed in hospitals where they can be properly treated. These patients with depressions formerly would be sick for three, six, nine, eighteen months, but today almost all of them can be cured or restored within four to six weeks, thus protecting them against the danger of suicide, and that is one of the things we can do for suicides. Many patients may not talk about suicide as such, but they tell you they feel like a failure, the family would be better off without them, that their whole life is worthless, and such expressions as that should make one realize they are contemplating suicide. The patients frequently do not come in saying they are blue, they say other things, inability to work, fatigue, peculiar feelings in the head, and lack of getting any satifsaction out of life. Often one has to ask them a direct question, if they are sad, or if they are happy, then the whole story comes out, they are depressed and melancholy. They frequently commit suicide without saying they intend to do so.

Dr. Johnson spoke of bromides and I wish to emphasize that. I find no need to prescribe bromide except once or twice a year and then only for brief periods. I know they are dangerous drugs to put in the hands of a patient; there are better sedatives than bromides. Often doctors will give a patient a prescription containing bromide and he is told to take it every three or four hours, then he phones back to say the medicine is out and the doctor tells him to have it renewed. Then the patient learns to have it renewed. Bromide is accumulated in the body, is not excreted as fast as it is taken in and this induces a toxic state which may cloud the underlying condition for which the bromide was given. If I had my way I would eliminate bromides completely from the pharmacopoea.

In the talk on alcohol, I find it is almost impossible to treat any of the bad cases of alcoholism without placing them in a hospital and frequently the general hospital is not suitable because the patient can leave if he wants to. Occasionally if you put one of those short hospital gowns on the patient and take away his other clothes, he is pretty well stymied. But he might even then wrap a sheet around himself and try to get to the closest bar. I never try to treat alcoholics at home for usually it is a waste of time. In ninety-nine cases out of a hundred, the patient has learned ways of getting around the family through practice extending over many years and there is no way to keep him from continuing to do this. It just does not work.

I withdraw alcohol completely and abruptly. I think it has a good psychological effect. When a patient comes to the hospital for treatment I tell him we can substitute something for alcohol and drinks will not be necessary. If you give small doses of alcohol for a few days it is harder to stop it. So I stop it when the patient is admitted to the hospital.

There is another emergency Dr. Johnson did not mention that I would like to say something about, and that is the patient who is markedly excited, the patient who cannot be controlled, who is breaking up the furniture, a danger to himself and everyone else. Often such a patient will not take medicine by mouth and some other form of medical control has to be devised. Bromides are too mild and too slow acting. I rely upon the use of morphine and scopolamine hypodermically. Morphine by itself will not have the desired effect, but

¼ gr. of morphine and 1/100 gr. of scopolamine will quiet practically any excited patient. After that plans can be made for hospital care and the regular administration of other drugs. Intravenous amytal sodium will be almost as satisfactory if you can keep the patient still enough to get the needle into the vein and give the drug slowly. Frequently you cannot do that because the patient is struggling and fighting.

ELECTROSHOCK THERAPY*

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Electroshock therapy is the generally accepted type of therapy, with its limitations, now used in the treatment of manic depressive psychosis, all types of psychotic depressions, and certain cases of schizophrenia, by most private psychiatrists and in most of the better state hospitals throughout the world. This type of therapy has definitely shortened the stay of the patient in a mental hospital. I have given electroshock therapy to an average of 50 patients, continuously, twice a week, for the past seven years, from December 1, 1940, to date. The following eight points are excerpts from GAP's article on psychiatric treatment† with which I heartily agree:

1) There is as yet no adequate theory on the mode of action of electroshock therapy. All indications are that it acts on a symptomatic, rather than on an etiological level.

2) The preponderance of evidence points to the conclusion that electroshock therapy materially shortens the majority of depressive episodes, particularly those that occur in the involutional period. It often aids in shortening manic episodes.

3) The evidence is conflicting as to the efficacy of electroshock in schizophrenia. Good results have been reported in some cases of severe catatonia and in some acute paranoid reactions.

4) Use of electroshock therapy is contraindicated in the psychoneuroses, with the possible exception of a reactive depression.

5) The complications and hazards of the use of electroshock therapy should be reemphasized, since they have been minimized by some workers.

6) The therapy should be given by psychiatrists only, and they should be well trained in the technic of its administration. It should be considered only as an addition to the total psychiatric treatment program.

7) The therapy should be given only to hospitalized patients, and never to private office patients.

8) Active research is still indicated, considering:

(a) The establishment of uniform criteria for evaluation of results of this type of therapy.

(b) Combined psychological and psychodynamic studies, which would lead to a better understanding of the patient.

(c) Adequate, long time follow-up studies, which would lead to a better evaluation of the patient's clinical status during a remission or after an apparent recovery.

To understand this type of therapy properly, a few words are now in order as to the cause of a psychosis. In plain words, other than lues, we just do not know. We cannot, therefore, consider electroshock therapy a true cure. In the psychotic patient, we know that there is, or has been, a reaction to the environment. Something happens to upset the patient's nervous system. He does not care to discuss this with anyone, so buries the conflict in his heart and begins to worry about it. The mental upset, brought about by the worry, plus some as yet unknown factor (possibly hereditary in nature) brings about the psychosis.

The electroshock produces a convulsion. Following it, there is a state of mental confusion, which varies in length, depending on the individual patient, from a relatively short time to several hours. The patient cannot worry about the reaction to his environment, whatever it may be, during the period of mental confusion. The therapy

* Read at the meeting of the Sixth District Medical Society (Louisiana) at the East Louisiana State Hospital, Jackson, Louisiana, November 7, 1947.

†Bulletin published by Group for the Advancement of Psychiatry, Topeka, Kansas, dated September 15, 1947.

is repeated a number of times, with the hope that the patient's problems will get dimmer and dimmer in his memory and that he will eventually forget them, and, as a result, will be restored or at least improved mentally. At this hospital, we give a minimum of eight or ten treatments and a maximum of twenty-five, consecutively.

After receiving the maximum number of consecutive treatments, the patient is given a rest period of about six weeks. If we then feel he needs more treatment, another series is started. Here, we never give up a case as unimprovable until the patient has had at least seventy-five treatments, or three complete courses. We give treatments twice a week. From January 1 to October 1, 1947, I have completed the therapy on 197 patients. Of these, 125, or 68.59 per cent, are at home on furlough at this time. We do not have a large enough social service department to do any follow-up work on furloughed patients, so I do not know how all of these 125 patients are adjusting away from the hospital. I do receive gratifying reports, occasionally, from some of these patients' relatives.

There are certain potential dangers from the electroshock treatment. As previously stated, it causes the patient to have a convulsion, and, during it, it is possible, though improbable, for the patient to sustain a fracture. The usual site of injury is a compression fracture of the dorsal spine. A few deaths have been reported, but these have occurred when serious complications follow the administration of electroshock therapy. As far as is known to the writer, there have been no fatalities as a direct result of the use of the electroshock therapy.

Because of the potential dangers, we, at the East Louisiana State Hospital, have required the written permission of the nearest of kin before the therapy is administered to any patient. In the immediate past, however, the Superintendent has given the writer his verbal permission to administer the therapy to any patient whom he considers a fit candidate, physically as well as mentally, with or without the written permission of the family. It is my understanding that a written permit is not required by many psychiatrists in private practice. From my point of view, it is really not necessary, for, as stated above, the electroshock therapy is the accepted method of treatment for various types of psychoses. Personally, I have not had a death as a direct result of the therapy, and the total number of broken bones is nine. Of these, seven were compression fractures of the dorsal spine, one was a fracture of the clavicle, and the ninth a chip fracture of the head of the femur.

Now, regarding the therapy itself: At this hospital, no food or drink is given the patient for about two hours, preceding the treatment, to lessen the possibility of aspiration pneumonia. The patient lies on his back, on a wooden table, with a pillow under the lumbar spine. A cloth gag is placed in the patient's mouth and the jaws are held together by a nurse. She also holds the patient's left shoulder and does not allow it to move about freely during the convulsion. An attendant holds the patient's left hand and left hip, another his feet, a third one holds his right hand and right hip and a fourth his right shoulder. Electrode jelly (one tube of KY jelly and one teaspoonful of salt) is applied to the patient's temples. The electrodes are placed on the patient's temples, and held with a rubber band. The machine is connected to the electrodes and the treatment is given.

The modern electroshock machines are so constructed that an overdose of electricity is practically impossible. The voltage can be controlled by turning a knob on the machine, from zero to the voltage on the line at the time the treatment is given. The newest machines have a booster unit on them, which will raise the voltage twenty-five volts over that on the line. The duration of the shock can also be controlled by turning a knob on the machine, from one-tenth of a second to one second. When the proper time and the proper voltage are reached (this varies with each patient), the patient immediately has the convulsion. this lasts a minute, or less, and the patient then often sleeps for about fifteen minutes

and awakens mentally confused. We start the therapy, at this hospital, generally, at 110 volts for six-tenths of a second, and give a double shock, for we have found that this will usually produce the desired convulsion. If it fails, the voltage is raised to 120, and a second attempt is made the same day. If no convulsion occurs after the second trial, nothing more is done until the day the therapy is administered again, when the first attempt is 120 volts for six-tenths of a second. As soon as the convulsion is over, the pillow is removed from the lumbar spine area and is placed under the patient's head. When the respiration has started again, the patient is moved to a bed, on a rolling stretcher, and the next patient is brought to the table. With our system, I administer treatment to 50 patients in approximately two hours.

Another type of therapy, electro-narcosis, is now coming into use in many places. This is a longer shock, but with a lower voltage, and encouraging results are being reported from its use. This type of electroshock therapy may soon be used in this hospital.

DISCUSSION

Dr. C. S. Holbrook (New Orleans): I am indeed glad to discuss the splendid work that Dr. Sturm and other members of the medical staff are doing in the East Louisiana State Hospital. That institution always begets fond memories for me, for it was there I received my early training in psychiatry.

The presentation tonight well illustrates the modern methods that are used to restore patients and greatly shorten their hospitalization. True, all psychotic patients are not benefitted by electroshock therapy, as exampled in the organic psychoses such as paresis, cerebral arteriosclerosis, and senility.

In New Orleans we have been using electroshock, or, as I prefer to call it, "electric-sleep," treatment since 1941. The group of us who practice at the DePaul Sanitarium, New Orleans, have administered 27,778 treatments to 3,831 patients; at Touro Infirmary I have given 8,347 treatments to 1,571 patients. There have been no deaths, and few serious complications as a result of the treatments.

Recently I studied 200 depressed patients who were treated at the DePaul Sanitarium before the advent of electro-sleep therapy, and it was found that many of these patients remained hospitalized six, twelve, eighteen months or more; the average stay was one hundred and twenty six days. Another group of 200 depressed patients, treated within the past six years with electro-sleep therapy, was compared with the previous group, and except for the employment of electro-sleep therapy these patients received essentially the same care and treatment. In this last group practically all the patients were restored within two months, and more than one half of that number were restored within thirty days. The average hospital stay was thirty-eight days as compared with one hundred and twenty-six days for patients treated without the benefit of electro-sleep therapy.

Another study was made of manic patients, and the results paralleled those of the depressed group.

With this modern therapy in properly selected patients, hospitalization time can be reduced by two-thirds or more, thus permitting a great hospital like this to treat many more patients in a given time because the duration of the psychosis could be markedly shortened.

In the less severe depressions, many individuals can be treated as out-patients. At Touro Infirmary, about 90 per cent of the patients receiving electro-sleep therapy treatment do not stay in the hospital but report there for treatment 2 or 3 times a week. They are admitted at 8 A.M., receive their treatment, and are able to leave by 9:30 or 10 o'clock. In the afternoon and evening, many are able to do their housework or go to picture shows, etc.

Dr. Sturm and the staff of the East Louisiana State Hospital are doing most creditable work, and I want to congratulate them and the Superintendent, Dr. Glenn Smith, who by his encouragement and cooperation has made all this possible.

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GENETICS AND CANCER*

WALTER J. BURDETTE, Ph. D., M. D.†

NEW ORLEANS

Among the unsolved problems in medicine, that of the etiology of cancer is one which remains most obscure, and the facts which have been learned about it bring forth new questions which are unanswered in addition to leaving the original problem only partially solved. In spite of prodigious effort, the patient with cancer can be offered much less than is desirable. Many feel that the real hope is to be found in

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fundamental research in oncology and that advances in treatment will follow additional knowledge so obtained. There is one phase of this approach toward which we would direct your attention. It is a consideration of the part heredity plays in initiating cancer.

GENERAL CONSIDERATIONS

Several questions present themselves when the genetic basis of susceptibility and resistance to cancer is considered. Do genes play a part in the appearance of cancer? Are one or more genes involved? Are the same hereditary factors involved in all types of cancer? What is their distribution on the chromosomes? Must the same gene be present on one or both chromosomes in each pair to be effective? How are the gene and its expression affected by changing the environment? These questions may be answered in part.

Before the genetic background of cancer development can be understood properly, it is essential that one knows how the units in heredity, the genes, are expressed. It is well known that the visible expression of a gene, the phenotype, depends on the conditions existing during the period of gene action. The effects of a gene may vary with environmental conditions, but the gene itself passes from generation to generation in unchanged form. It follows then that the end result of gene action in an organism does not necessarily indicate the presence or absence of the gene on a chromosome. Applying this to cancer, we must study susceptibility to cancer and not regard the presence or absence of cancer as necessarily indicating the presence or absence of these genetic factors for susceptibility. A consideration of the effect rather than the genes for susceptibility themselves led to erroneous interpretation of Slye's data[21] on cancer in mice.

There are many instances of familial incidence of cancer in man, but the most convincing data that there is an hereditary background are found in studies on other forms, particularly mice. This is in large part due to the heterogeneous nature of the human population and obvious lack of proper control in an experimental sense. By inbreeding, it has been possible to produce strains of mice which are remarkably uniform in their susceptibility to certain specific neoplasms appearing spontaneously and induced. These stocks are the most uniform mammalian population yet produced, and until these strains were established by brother-to-sister matings through a single line for many generations, progress in the experimental study of cancer was retarded. After they became available, advancement in our understanding of the origin of neoplasms was more rapid, and this application of genetics has generally been credited as a significant step forward. Experiments designed to yield information about the chain of events leading up to the neoplastic change have been most fruitful.

TUMORS INDUCED BY SUBCUTANEOUS INJECTION OF CARCINOGEN

In order to show how genetic factors for susceptibility operate, let us first examine one example[5, 6, 7] in detail and then compare these results with those for other types of tumors. The case of induced, subcutaneous tumors in mice is representative in some of its aspects and unique in others. Induced tumors were studied because they appear earlier and much more frequently than spontaneous tumors of the same type.

The method of study used was to inject each mouse at sixty days with 1.0 mg. of 20-methylcholanthrene, a carcinogenic hydrocarbon. The needle was introduced subcutaneously. The animals were given a uniform diet and maintained in air-conditioned quarters. The time of appearance and nature of the tumors were noted.

The incidence of tumors was studied first in a number of inbred strains. Tumors appeared at the site of inoculation, and microscopic examination of the tumors showed neoplasms of four primary types. They were spindle cell sarcomas and rhabdomyosarcomas chiefly. Epidermoid carcinomas and anaplastic tumors were found occasionally. In addition two or three of these elements were present in the same section at times. The tumors were malignant and autonomous as demonstrated by transplan-

tation experiments. Also autopsy showed invasion of the body wall.

It is clear that there are differences in the susceptibility of the groups, since environmental conditions were held relatively constant. In general a larger total number of animals have tumors if the time of tumor appearance is earlier. It is important to know that even if an animal does not develop a cancer, its offspring have tumors in a percentage of cases characteristic for that stock. Further proof that heredity plays a role is that the susceptibility of the more closely related strains is similar.

By mating mice of the most susceptible to those of the most resistant strain, the nature of the inherited factors for susceptibility is made clearer. If a completely dominant factor for susceptibility were present, one would expect all of the offspring to develop cancer in the same manner as the most susceptible, C_3H strain. If a single, completely recessive factor were present, the offspring should have the same incidence of tumors as the most resistant, JK strain. It is evident from the data that neither of these possible conditions is present. This intermediate type of inheritance is known to exist for other inherited characters besides susceptibility to cancer and may best be explained by the presence of multiple genes. That is, a number of genes contribute to the total effective susceptibility but each not necessarily to the same degree. Matings result in offspring with intermediate expression of the character. It is probable then that multiple genes determine susceptibility to these tumors which have been described.

There was no difference in susceptibility between males and females. When the reciprocal cross was made the offspring of the more susceptible females had no greater tendency to develop tumors than those of the more resistant females. It was this type of cross which led to the discovery of the milk agent in mammary cancer in mice. There is no evidence that such a substance plays a role in the origin of the tumors under discussion.

It is possible to find whether genes for susceptibility are present on chromosomes known to carry other genes unrelated to cancer. The JK mice bear four mutant genes, *pink eye, short ear, non-agouti,* and *brown.* If animals showing any of these recessive characters in the backcross generation are more resistant than those with the normal allele, genes for relative susceptibility to cancer reside on that chromosome. However, this was not the case and therefore there is no evidence that the genes involved in the inheritance of cancer are present on these four chromosomes. Results in other laboratories on different types of tumors indicate that genes for susceptibility are present on the chromosomes carrying *brown* and *non-agouti* and the X-chromosome, so it is possible to say that identical genes are not involved in susceptibility to all types of cancer.

From these studies we may conclude that susceptibility to tumors induced with methylcholanthrene is hereditary in certain strains of mice. The differences found are in appearance time of the tumors, survival time of mice developing tumors, and the predominant type of tumor. Survival time does not necessarily parallel susceptibility as judged by the appearance time of induced tumors. There is no evidence that a milk agent affects the appearance of the neoplasms. Susceptibility to cancer in the mice studied is due to multiple genes which are present on chromosomes other than the sex chromosomes or chromosomes 1, 2, 5, or 8.

OTHER TYPES OF CANCER IN ANIMALS

By similar methods other types of inheritable cancer have been studied in mice. It should be interesting to compare the results reported above and those obtained in other types of cancer by other investigators. Perusal of the literature yields abundant evidence that genes for cancer susceptibility are linked to definite chromosomes. Melanotic tumors in insects and fish[8] appear when certain genes are present. It is interesting that even in so simple a form as the fruit fly the situation is complex, and several genes on different chromosomes are involved.[9, 20, 22] *Neurospora* was selected by Beadle, Tatum,[2] and others to study gene

action in a relatively simple organism. They have found a one-to-one relationship between mutant genes and the chemical reaction selected for study. It is interesting that some of the same agents which are effective as incitors of cancer also cause mutations[1] in *Neurospora*, *Drosophila*, and possibly mice.

Heston[10] believes that susceptibility to pulmonary tumors in mice is due to multiple factors, and he has located and identified them on two chromosomes and ruled out several other chromosomes as the location of others. He also found susceptibility increased by the lethal yellow gene which may be associated with increased body size in these animals.[11] Little[17] found that yellow mice had a lower incidence of mammary cancer than non-yellow mice in crosses between susceptible dilute brown mice and resistant yellow mice. Bittner[4] decided that multiple factors are responsible for susceptibility to mammary cancer and concluded that one may be linked to the chromosome bearing brown in studies on C_{57} and A mice.

In breeding experiments it was found that the offspring of females from a strain with high incidence of mammary cancer had approximately as many tumors as the parental females, even when the male parent was of a strain in which few of these tumors appeared. However, when the reciprocal cross was made, the incidence in the F_1 was much lower. That is, when the female parent was from the resistant strain and presumably the male of the susceptible strain introduced only chromatin into the F_1. This difference was attributed to an extrachromosomal factor by Little and coworkers[14] and Kortweg.[16] By means of foster-nursing experiments, Bittner[3] was able to show that it resided in the mother's milk. The presence of milk agent, however, does not eliminate heredity as being operative in cancer genesis, and there is evidence to show that even the milk agent is influenced by genetic factors. Mice may develop mammary carcinoma after the milk agent has been eliminated. A third thing which is known to influence the appearance of mammary cancer is the hormonal mechanism and accounts for differences in incidence of this cancer in males and females. Thus several mechanisms play a role in the origin of mammary cancer in mice, and hereditary factors are probably effective in two ways, primarily on the organism and also secondarily through their effect on the hormonal and milk factors.[12]

Cancer of the stomach has been induced in mice with carcinogens. The forestomach is lined with squamous epithelium and tumors appearing there have no similarity to carcinoma of the stomach in man, but adenocarcinomas also appear. Strong[23] has developed a strain which develops adenocarcinoma of the stomach spontaneously and has reported that it is due to an inherited factor on the chromosome bearing the gene for brown coat color. This NHO strain was formed by serial administration of carcinogen to mice of successive generations not highly inbred originally. Animals resistant to subcutaneous tumors were selected, and eventually in one subline adenocarcinoma of the stomach began appearing in a predictable fashion without the injection of carcinogen.

Spontaneous leukemia appears in many animals and has been studied most extensively in fowls and mice. Myelogenous leukemia and erythroleukemia are transmissible by a virus in fowls. All forms of leukemia occurring in man are also found in mice except for plasma cell leukemia. Inbred strains of mice such as the C_{58} strain of Richter and MacDowell[19] have been produced and shown to develop leukemia in a characteristic percentage of the animals. Most of the animals developing the disease have the lymphogenous form. Studies on the inheritance of leukemia show that in strains where leukemia occurs, even those not having leukemia have a characteristic number of offspring with the disease. Multiple genetic factors may account for susceptibility to the disease. There is good evidence that a maternal non-chromosomal factor has an influence in its development, but this agent is not carried in the milk. No difference in sex incidence is present. The incidence of leukemia is increased and man-

ifestations accelerated by carcinogens, estrogens, and x-rays. However, mice developing leukemia are not susceptible to all agents to the same degree and may be resistant to one and susceptible to other leukemogenic treatments.[15]

GENETICS AND CLINICAL CANCER

Transferring conclusions reached from studies on other species to man must always be critically and carefully considered. There is enough suggestive evidence that hereditary factors are important in the occurrence of human cancer, however, to indicate that basically a similar situation may exist in both. Characteristic racial incidence of cancer at the various sites is well known. For example, Iguchi[13] reports a relatively low incidence of mammary cancer in Japanese women. The Norwegian Cancer Committee collected 6,000 cases of cancer and interviewed the relatives.[24] They found the incidence of cancer higher among sisters than wives of the patients with cancer. If one parent had cancer, more than twice as many of the siblings had cancer as when neither parent was affected. Doubtless retinoblastoma is an inherited disease at times, usually appearing in successive generations.[25] Additional evidence of an inherent susceptibility is the bilateral distribution in 20 per cent of those affected. Neurofibromatosis appears in families and in many is inherited in the manner of a dominant character. Rectal polyps often undergo a malignant transformation, and very striking family histories have been published by Lockhart-Mummery and Dukes[18] showing that multiple polyposis is inherited in a dominant fashion. One example given is a set of twins who developed symptoms at 30 years and both died at the age of 41, one from intestinal cancer and the other as a result of colectomy for adenomatosis.

Anyone familiar with Rh blood grouping will agree that it is not necessary to defend the importance of heredity in the management of some diseases. Although at the present time it is not possible to state exactly how genes operate in the etiology of cancer, knowledge that they play some part should be utilized. There are several ways in which this can be done. If a patient has a neoplastic disease known to have a high familial incidence, his physician should inform him so that he may decide about questions of marriage and having children with that in mind. The relatives (children, siblings, and parents) of patients found to have polyposis of the colon, or carcinoma of the colon appearing as a later manifestation of that disease, should have sigmoidoscopy and barium enema performed at least. Where there is any doubt in the clinician's mind as to whether further diagnostic procedures should be done in a given case, a suggestive family history of cancer should be taken into consideration. For these reasons a family history is an important part of any patient's record and should be taken carefully. There is no conclusive evidence that a milk agent for cancer is present in human milk. Pertinent data should be included in the history for future reference, but artificial feeding is hardly indicated as a measure to prevent breast cancer at the present time. With this brief discussion of one phase of our knowledge of the cause of cancer, it should be evident that there are a number of avenues of approach to the problem which should allay in part the usual pessimism which pervades this field.

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HEALTH UNITS FOR LOUISIANA

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NEW ORLEANS

The health of the people has always been the responsibility of the physician. His is the responsibility both for the prevention of illness and for treatment should illness develop. The growth of population and accumulation of people into larger communities has brought with it different and more complex problems in prevention. The safeguarding of their health has become less a personal problem and more and more of a community responsibility; thus, the development of Public Health as a governmental function as well as a branch of medical practice. The public health physician is concerned with the health of communities and the broader aspects of disease, morbidity and mortality rates, and environmental protective measures. His specialty requires the cooperation of the sanitary engineer, the public health nurse, the statistician, the epidemiologist, and other technically trained personnel, and above all the spirit of the missionary.

The modern public health movement was founded upon the discoveries of the last six decades in the field of bacteriology. With the discovery of the etiological agents of many of the infectious diseases and their mode of spread, it became possible to institute preventive measures, such as water purification, sanitation, and food protection. It ushered in a new era in preventive medicine as well as in curative medicine.

During the past few years there has been remarkable progress in the field of preventive medicine as well as in curative medicine. There has also been an awakening of community consciousness and interest in the broader phases of prevention and control of disease. This movement has been led by the physicians individually and through their organizations, both state and national. Physicians in private practice are working more closely than ever in cooperation with community leaders and public health personnel to give to the people the greatest benefits ever known in the preservation of health and well-being.

NATIONAL HEALTH PROGRAM OF THE A.M.A.

Perhaps the greatest stimulus of all in this direction has been the National Health Program of the American Medical Association which was adopted and promulgated by the Board of Trustees and the Council on Medical Service in February of 1946. Since our topic has to do with adequate health services especially through Parish Health Units, it is pertinent to quote from Point Number Two of this ten point program: "The provision of *Preventive Medical Services* through professionally competent health departments with sufficient

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staff and equipment to meet community needs is recognized as essential in a health program. The principle of federal aid through provision of funds or personnel is recognized with the understanding that local areas shall control their own agencies as has been established in the field of education. Health departments should not assume the care of the sick as a function, since administration of medical care under such auspices tends to deterioration in the quality of the service rendered. Medical care to those unable to provide for themselves is best administered by local and private agencies with the aid of public funds when needed." Coincident with the development of this program and following it, state and local medical societies have planned for the strengthening and expansion of health programs in their respective areas.

LOCAL HEALTH UNITS FOR THE NATION

Public Health administrators the nation over have been interested in more efficient organization of their departments and their services. The acknowledged shortage of professional personnel including those trained in public health and the increasing cost of services have made planning for efficient organization necessary, if expansion is to proceed along rational lines. A most extensive study on this subject was made by a committee of the American Public Health Association. This study has been reported in an exhaustive report entitled "Local Health Units for the Nation." This report has been revised in some respects since it first appeared and stands as the most comprehensive appraisal of health organization and standards for personnel extant. It has been the stimulant and the model for state planning since its appearance.

The report develops the principle that for efficient service, health units should be organized not solely on the basis of political subdivisions but on population groups of a size that can support such an organization. A population of fifty thousand has been set as the smallest able to support an adequate health service. The cost of maintaining an adequate service would be too great for a smaller group and in most instances could not be afforded. It is estimated now that adequate local health service, based on the standards for personnel set up in the report, costs approximately $1.50 per capita per year. For an area with less than fifty thousand population the per capita cost would be greater so it is recommended that parishes (counties) be grouped where necessary into health districts with a population large enough to support an adequate service.

The report recommends certain standards for personnel on the basis of population. It is considered that adequate local health service can be rendered by one public health physician for each fifty thousand population, one public health nurse for each five thousand population, one sanitarian for each fifteen thousand population, and sufficient clerical personnel to handle the work of this staff, or one clerk for approxmately each twelve thousand population. Thus for an area of fifty thousand population the staff would consist of one physician, director of the unit, ten public health nurses, three sanitarians and four or five clerks. These ratios would of course vary to some extent with the area served and its problems and programs. Certain areas may require a larger staff of sanitarians. Such would be true of an area with a large food processing industry. Also an area with a smaller population than fifty thousand may be more efficiently operated as a unit with a full time public health physician than if it were combined with another area just to bring the total population to the suggested minimum. No standard can be strictly adhered to but must be adjusted to suit the conditions of the particular area concerned.

THE ROLE OF THE PUBLIC HEALTH PHYSICIAN

We must recognize the fact that the public health physician is essentially a medical administrator with a thorough knowledge of the mass phenomena of disease prevention and health promotion. He need not often himself be a specialist in pediatrics or obstetrics, vital statistics, or even in epidemiology. He is first of all a specialist

in public health, but remains largely a general practitioner of public health.

Like any good administrator, the physician in public health must have a full knowledge of what the specialities and specialists in medicine can contribute to his objectives. He will need part-time or even full time specialist-physicians on his staff. But the medical director of an industry need not necessarily be a surgeon, or even an internist. He does need to know how to select good surgeons, and what to expect of them. The health officer, if he is a good administrator, must know how to select specialists as needed. Of prime importance is his knowledge of what to expect of them and how to provide a congenial working environment which will offer them the satisfaction they seek and make their services most valuable to the public.

No one but the public health administrator himself can provide complete knowledge of, and give constant attention to, the health problems of large groups of the population; the most effective methods of improving their mental and physical health; the dangers of their environment and methods of mitigating those dangers; effective methods of presenting his needs to the public and to fiscal officers; and the science and art of personnel administration.

These necessary knowledges and skills are acquired through special training and experience just as are those needed by the specialist in other fields of medicine. The public health physician must be considered as one of the team of medical practice which as a whole is responsible for health for all.

PROPOSED PUBLIC HEALTH ADMINISTRATION IN LOUISIANA

In planning for public health administration in Louisiana, it is considered that local units of jurisdiction should include a sufficiently large population to support and to justify a staff of full-time, professionally trained persons. Accordingly, to provide for the efficient use of personnel, it would be desirable to decrease the number of local health units in the State by the formation of health districts in lieu of certain individual parish health units. Legislative authority for such health districts already exists in Act 79 of 1921 as amended and Act 246 of 1942, the Local Service Act.

The combination of parishes into districts which has grown out of this planning is shown in Table I. In preparing this plan consideration was given to various factors, including population characteristics, distribution of population within the parishes, and accessibility of the parishes to each other over the existing highway system.

The proposed arrangement should be considered tentative. In the development of the program consideration will, of course, be given to the views of the local agencies which contribute funds and support to the local health units.

TABLE I

A PLAN FOR DISTRICTING LOUISIANA FOR THE ADMINISTRATION OF PUBLIC HEALTH SERVICES

DISTRICT NUMBER	PARISHES	ESTIMATED POPULATION
1	Caddo	141,572
2	Bossier, Webster	65,011
3	Claiborne, Bienville	40,432
4	Lincoln, Union, Jackson	49,176
5	Ouachita, Morehouse, Caldwell	94,501
6	East Carroll, West Carroll	29,707
7	Richland, Franklin	50,501
8	Madison, Tensas	26,382
9	DeSoto, Sabine	42,600
10	Natchitoches, Red River	46,294
11	Winn, Grant	29,076
12	LaSalle, Catahoula, Concordia	36,926
13	Vernon, Beauregard	50,495
14	Rapides, Avoyelles	139,023
15	Calcasieu, Cameron	97,225
16	Jefferson Davis, Allen	40,030
17	Evangeline, St. Landry	100,277
18	Acadia, Vermilion	85,081
19	Point Coupee, W. Baton Rouge, Iberville	53,601
20	E. Baton Rouge, E. Feliciana, W. Feliciana	144,382
21	St. Helena, Livingston, Tangipahoa	64,850
22	Ascension, St. Charles, St. James, St. John	57,527
23	Washington, St. Tammany	57,689
24	Jefferson, Plaquemines, St. Bernard	96,107
25	Orleans	609,575

It is considered that the proposed organi-

zation would provide an efficient and effective administrative program for the present; and will provide also a program for orderly progression and advancement of personnel of various kinds in the health services of the state.

FINANCIAL SUPPORT OF LOCAL HEALTH UNITS

An important part of the planning has been the matter of financial support of local health units and distribution of State and Federal funds. Under the American form of government sovereignty is vested in the State. State agencies and local governmental units get their authority to exist and to function by delegation of authority and power from the State, as provided in the State Constitution and in Acts of the Legislature. Public health administration is but one of many governmental functions, and local units of government in Louisiana by the Constitution and by legislative act have both the authority for local health administration and the responsibility of supporting this function.

Public health administration is based upon, and is an exercise of "Police Power," an inherent attribute of sovereignty. Delegation of authority by the State to local units of government does not divest the State of its authority, or relieve it of its responsibility to protect its citizens. The complex, frequent, and close contacts incident to present conditions make it difficult, and in fact impracticable, to define exactly and to delimit precisely all matters of strictly and purely local sanitation, not affecting other portions of the state. Therefore, the State should give assistance, including financial assistance, to local boards of health; and in the event of failure, refusal or inability of local agencies to provide protecttion, the State is obligated to provide at least a reasonable degree of protection commensurate with its financial ability and local needs.

The State has for many years been giving assistance to parishes for the organization and maintenance of health services. There has, however, been no set procedure for the allocation of State and Federal funds, so that all parishes have not shared equitably in this assistance. It is proposed that a formula be developed for this purpose and such is under study at the present time. In developing such a formula consideration is being given to a *basic local appropriation* to be equivalent to a fixed proportion of the Parish property tax; an *equalization* allocation of State funds, where necessary, to bring the basic local appropriation to a set per capita amount; and a *matching allocation* of State funds to match in certain ratios the local appropriation. It is felt that such a formula for distribution of State and Federal funds will result in more stable and efficent organization of local health services.

The foregoing is the direction taken by your State Health Department in planning for organization and services through Health Units. Such planning is primarily the province of the public health administrator, but in this he and the practicing physician can meet on common ground, and by sustained and organized effort attain more readily the ultimate goal of optimum health for the individual and the community.

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THE BCG VACCINE

Tuberculosis must be fought. The battle against it has to be waged by the individual practitioner, by hospitals and institutions, by employee groups and by community welfare campaigns. There is an increase in tuberculosis after every war. Physicians and the public are more conscious of tuberculosis now than in the past. This is due to the recent recognition of the increase following war and to the campaigns in which masses of people have been surveyed with a roentgenogram of the chest.

In this collective effort to control tuberculosis the position of the BCG vaccine is of pressing concern to the physician and of interest to the public. In 1906 Calmette isolated a strain of tubercle bacillus from the milk of a tuberculous cow. After many subcultures and much animal experimentation a comprehensive paper was published in 1920 by Calmette and Guerin. In this it was indicated that the organism with which they were working had lost its virulence, was nontuberculogenic, incapable of producing generalized tuberculosis in guinea pigs and cattle but retained antigenic properties and had afforded some degree of protection to inoculated animals. The organism came to be known as *Bacille Calmette-Guerin,* and ultimately, the product as the BCG vaccine.

The results of the first clinical trials in 1924 in France were not statistically convincing to scientists in various countries. Subsequent trials were instituted in various places. The interest was marred at this time by one major (Lubeck, Germany), and two minor disasters (Hungary and Chile) in which tuberculosis followed the administration of the material. These disasters have been shown to be the result of contaminations and not from a return of virulence of the organism. The effect was to increase skepticism.

In the twenty odd years in which the vaccine has been used and its effects discussed there has been much controversy as to its safety and value.

The vaccine has been used in South America, has been given to over 5,000,000 individuals in Europe. It was used extensively in Norway before and during the War. It has been used in various places in this country but received generally here with some caution.

For clarification of the situation, Frederick Tice instigated a comprehensive experimental and clinical study in 1935. It was carried out by various interested groups in Chicago under the direction of Rosenthal and others. After ten years it was stated that in "2,831 new born infants living in the poorest districts of Chicago, but not in household contact with tuber-

culosis, there were 11 cases of tuberculosis in the vaccinated against 39 in the controls. In 256 new born infants, when tuberculosis was present in the household and when isolation in foster homes was practiced in the controls and vaccinated alike, there were 2 cases of tuberculosis in the vaccinated as compared to 5 in the controls. The rate was 4.56 times as great in the controls. There were 4 deaths in the controls and none in the vaccinated."

Two years ago a conference was held under the auspices of the United States Public Health Service to consider the situation in the light of reports such as that given above. It was recommended that BCG vaccine not be made available commercially at present, that extensive investigations be carried out. The American Trudeau Society has advised care and caution in preparation and utilization. They consider that general vaccination is not desirable but that individuals or groups especially vulnerable should be vaccinated —provided they do not react to adequate tuberculin tests.

All are cautioned that immunity is only relative and that all established means of protection and control are important to the vaccinated groups and to the community.

It is stated that there are more than 500,000 cases of tuberculosis in the United States and there is an annual mortality of 50,000. Accordingly, a resource that is apparently safe and may be protective should be given an extensive trial and should be made available to the vulnerable groups.

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Q FEVER

In 1935 an outbreak of an unknown fever was observed in Brisbane, Australia. An investigation by Derrick and by Burnet and Freeman established the entity now known as Q fever. The disease occurred in the workers of a meat plant. Nine typical cases were described in the first publication. It was shown that guinea pigs were susceptible to the disease and could be infected by inoculations of blood or urine from patients during the active phase of the disease. Burnet and Freeman found rickettsial organisms in the liver and spleen of mice inoculated from guinea pigs. The illness was acute. The first complaints were headache, pain in back and limbs, and fever. Mild respiratory symptoms were present in some cases. Leucocyte count was within normal limits and the illness was variable in duration. Milder cases had fever for about nine days; others up to twenty-four days.

In 1938, Davis and Cox reported the recovery of a filter-passing infectious agent from ticks near Missoula, Montana. This organism was later proven to be identical with that found by Burnet and it is now known as *Rickettsia burneti*. Outbreaks of fever and illness caused by this organism have occurred twice in the National Institute of Health and in two laboratories in Australia. During the latter part of World War II outbreaks of Q fever were reported in the Mediterranean area, in Panama, in a military unit returning from Italy to Virginia. In March 1946, Q fever occurred in Amarillo, Texas, among a group employed in the meat industry. In August 1946, a similar outbreak appeared in the employees of a packing house in Chicago. An endemic area of the disease was found in southern California in the spring of 1947.

Much investigation has been done to discover the reservoir and the method of transmission of the disease. The presence of infection is known to exist in certain ticks and small animals of Australia and in certain ticks in the United States. A serological study of over 2000 cows in the Los Angeles endemic area revealed approximately 13 per cent possessed antibodies against Q fever. The *Rickettsia* could not be recovered from the blood, urine, or feces of the cow but were found in raw milk. Pasteurization sterilized the milk but it was not felt that drinking of raw milk was responsible for the majority of human infection. The various outbreaks have occurred mainly in meat workers and labor-

atory workers and in units of military personnel.

The symptomatology and physical findings of the various outbreaks of the disease are similar but would not be susceptible of diagnosis without laboratory means. Pneumonitis was recognized first in 1940. In a certain outbreak in the National Institute of Health there were 45 cases. The incubation period varied from twelve to twenty-three days; there were 13 women and 32 men; their ages were from 18 to 64. The majority complained of headache and general aching, about one-third complained of cough. A few complained of nausea, vomiting, bloody sputum, diarrhea, and constipation.

Among the signs of significance, 32 had chills, 11 rales in the chest, and 10 had fever without chills or sweating. A few had signs of pulmonary consolidation, or conjunctivitis, or dyspnea. In 13 patients there were physical or x-ray signs of pneumonitis; in 32 there was no evidence of pneumonitis. In the latter groups the severity of the illness varied widely. The fever persisted one to fifteen days, the average was about six days. The routine laboratory studies did not point the way to diagnosis. The total leucocyte count was normal except in one patient with pneumonitis in whom it was 18,000 with 86 per cent neutrophiles. Diagnoses were confirmed by positive fixation tests. Sulfadiazine and penicillin were given to many patients having a severe form of the disease but without apparent effect. Other observers reported that fever subsided in ninety-six hours in one patient after streptomycin was given on the ninth day. In the Amarillo outbreak 11 of 18 hospitalized patients had normal temperatures on the twelfth day of illness without specific therapy.

It is seen that Q fever is an acute contagious rickettsial disease spread by means as yet unknown and appears thus far chiefly in localized outbreaks. The disease produces an acute toxemia of variable severity and also a pneumonitis in a certain proportion of patients. It is to be considered along with influenza, primary atypical pneumonia, and the bizarre types of pulmonary infections. It is evident that it will be of growing importance to the physician and he will require experienced laboratory assistance.

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ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

MESSAGES FROM THE PRESIDENT

PARISH MEDICAL SOCIETY

The real strength of organized medicine rests largely in the Parish Medical Society. This is the individual unit, which, added to many others, makes up the whole. The Louisiana State Medical Society is nothing more or less than a combination of the various parish medical societies. At the present time there are forty-five parish medical societies, organized and active. This should be increased so that every parish is organized as an individual unit or as a bi-parish or tri-parish medical society.

What should the Parish Medical Society accomplish, or what should its duties be? First, of course, it should bring a close, friendly contact between the doctors of the parish. Nothing helps more to establish friendly relations between doctors than parish medical society meetings where our common troubles can be freely discussed. We soon learn that we are all striving for the same goal and need each other's help.

Certainly the parish society should be of some educational value to the doctor. Scien-

tific discussion by members of the local group or by men from the surrounding territory, should accomplish this, and should be of distinct value. The papers or discussions should of course be practical and something of interest and value to the doctors in that particular parish.

As important as these functions are, a parish medical society has even more important duties. It should be the clearing house for all matters pertaining to measures for the improvement of the health and sanitation of the parish. Too often we have failed to make our position in this respect known to the public. Obviously the people of a parish will not seek the advice, or have confidence in a parish society which has not been active and has not demonstrated its interest in the general welfare of that community. Actually the parish society should study the needs of that community, and be the leader in these things, rather than follow the lead of some politician, society, etc.

One cannot help but realize that as a group, we must take a more active interest in such matters. There have always been a few doctors in every part of the state who have taken an active part and have been leaders in matters pertaining to health and the general welfare. This has been helpful, but would be far more effective if it came from the parish society as a body.

It is our hope that we will have an active medical society in every parish in the state, each affiliated with the State Society and each working so as to carry the influence of organized medicine into every part of the state.

M. D. Hargrove, M. D.

LOUISIANA PHYSICIANS SERVICE

It may be accepted as a fixed policy that the American people want some means of prepaying the cost of hospital and medical expense. Our answer to that is in providing an opportunity through voluntary insurance, both for hospital and surgical expense, which in time will be broadened to cover all medical and surgical expense.

Insurance to cover hospital expense is now on a very firm foundation, having been in use for a number of years. Many doctors looked upon it with some misgiving when it was started, but the great majority of doctors now accept it as a great benefit to their patients and to them. Certainly many an individual has had the burden of hospitalization materially reduced by hospitalization insurance.

Insurance covering medical and surgical fees was started later but in the few years it has been in force has had a very rapid growth. Now, practically every state has some plan of voluntary insurance sponsored by the State Medical Society or a component part of the State Society. Most of the plans have had some difficulties, as is to be expected when new fields are entered. Fortunately they have weathered the storm and generally are steering a smoother course.

The Louisiana State Medical Society started its plan, Louisiana Physicians Service, in the fall of 1946. We, too, have experienced some difficulties, most of which have been overcome, so that we now expect smoother sailing in the future.

It cannot be too strongly impressed upon the doctors of the state that Louisiana Physicians Service is your Company, started and backed by the State Society. It is your serious endeavor to offer to the people of the state a method whereby they can care for their surgical fees by prepayment insurance methods. For those in certain income groups, it covers the entire cost, and you, by becoming participating physicians, have agreed to accept the fee paid by Louisiana Physicians Service as your fee in full. For these people no other form of insurance will satisfy their needs. An indemnity plan for them simply does not go far enough.

In order for Louisiana Physicians Service to succeed and to meet the need for which it was started, it must have the ac-

tive support and cooperation of all doctors. It is your duty, as a member of the Louisiana State Medical Society, to see that the insured individual gets the protection he deserves under the policy. It is also your duty to be equally fair with *your* Company, Louisiana Physicians Service, and see that it gets a fair deal in each case.

You should also be an ardent booster of Louisiana Physicians Service. Whenever the subject of prepayment medical plans is discussed ,you should at once speak up for the part your society is taking in that movement. True, we only cover surgical fees at the present time, but you can truthfully say that we hope to broaden that to cover medical fees as we progress and acquire more experience. Louisiana Physicians Service is supplying a decided need in our state, and as it progresses, will be of increasing benefit to the people of Louisiana.

Be a booster of Louisiana Physicians Service, speak up for it, and help safeguard its interest whenever possible. It is your project, and it needs your support in every way possible.

M. D. Hargrove, M. D.,
President,
Louisiana State Medical Society.

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LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Natchitoches	Second Tuesday of every month	
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

SEVENTH DISTRICT SOCIETY

The Medical Society of the Seventh Congressional District will hold its fall meeting in Lake Charles, on Friday and Saturday, September 10 and 11. As usual, the Calcasieu Parish Medical Society will be host on this occasion. They are planning a full scientific program with distinguished guest speakers from out of the city as well as some of the leading physicians and surgeons of our state.

The Calcasieu Parish Medical Society is certainly to be congratulated on this effort to bring together not only the doctors of the Seventh District, but of outlying parishes and areas, to be the recipients of such a scientific treat. This statement is predicated on the fact that previous meetings similar in character have been outstanding scientifically and enjoyed by the great number of physicians who attended. We feel sure that the present meeting will exceed the efforts made in the past so that all who will attend shall be assured of a successful meeting.

Mark your calendar for September 10 and 11, Lake Charles.

The final program will very shortly be disseminated to all the physicians of the district and surrounding areas. You are urgently requested to avail yourself of this unusual opportunity.

NATCHITOCHES PARISH SOCIETY

A meeting of the Natchitoches Parish Medical Society was held at the home of Dr. Joseph Bath, President, on Tuesday, July 13. At this meeting Dr. M. D. Hargrove, President of the State Society, spoke. Dr. Bath presided at the business meeting, after which a delicious supper was served.

THE SOUTHERN MEDICAL ASSOCIATION MEETING

The forty-second annual meeting of the Southern Medical Association will be held at Miami, Florida on October 25-28 with the Dade County Medical Association as sponsor.

At a meeting of the Executive Committee on July 24, Dinner Key was selected as general headquarters for the following: registration; all section meetings, scientific, technical and hobby ex-

hibits; and motion pictures. Dinner Key (the former Pan American Air Depot) is ten minutes' ride from the general hotel headquarters and makes it possible to hold all of the above activities in one location. There is parking space for over a thousand automobiles around the main building.

The evening programs, which will include the General Public Session, the General Session and the President's Ball, will be held at the Municipal Auditorium. The auditorium is just off of Biscayne Boulevard and is only a short distance from the general hotel headquarters.

Hotel reservations will be handled by the Hotel Committee, Southern Medical Association Meeting, c/o City of Miami Convention Bureau, 320 N. E. Fifth Street, Miami 32, Florida. Since the meeting is being held earlier than usual, all requests for rooms should be made immediately.

REGIONAL CANCER CONFERENCE

The second Southwest Regional Cancer Conference will be held in Fort Worth, Texas on October 12 at the Blackstone Hotel under the auspices of the Tarrant County Medical Society and the Fort Worth Unit, Texas Division, American Cancer Society.

The one-day conference will consist of morning and afternoon lecture sessions, a clinical luncheon with an open forum question and answer period, and a public meeting in the evening.

Guest speakers at the conference will include: Dr. Chas. Huggins, Chicago, Professor of Surgery, University of Chicago; Dr. A. R. Curreri, Madison, Wisconsin, Associate Professor of Surgery, Wisconsin Medical School; Dr. James Barrett Brown, St. Louis, Associate Professor of Clinical Surgery, Washington University School of Medicine, and Associate Professor of Oral Surgery, Washington University School of Dentistry; Dr. Robert A. Moore, St. Louis, Professor of Pathology, Washington University School of Medicine.

There will be no registration fee. Further information about the conference may be obtained from the Tarrant County Medical Society, 209 Medical Arts Building, Fort Worth 2, Texas.

NATIONAL SOCIETY FOR CRIPPLED CHILDREN CONVENTION

The 28th annual convention of the National Society for Crippled Children & Adults, Inc., will be held at the La Salle Hotel, Chicago, November 15-17.

Many outstanding speakers in the fields of medicine, health and education will be on hand to present facts on progress in work with the handicapped during the past year, according to Lawrence J. Linck, executive director.

The convention will be attended by physicians, therapists, educators, workers with the handicapped and representatives of National Society's more than 2,000 states and local units throughout the United States, Canada, Alaska and Hawaii.

FOOD AND DRUG ADMINISTRATION

Druggists and the medical profession were urged today by the Federal Security Agency's Food and Drug Administration to return all stocks of Siliform Ampuls to the manufacturer, The Heilkraft Medical Company, Boston, Mass. This injection drug, which should be sterile, is potentially dangerous since samples collected on the market contain living organisms. Siliform is injected by some physicians and osteopaths in the belief that it will relieve patients suffering with rheumatism as claimed by the manufacturer. The Food and Drug Administration found the contaminated samples after a routine inspection at the Heilkraft factory disclosed that the Siliform Ampuls had been manufactured without sterilization. Intensive recall efforts by the manufacturer and the Food and Drug Administration for the past two weeks have not brought in all of the contaminated stocks. The article, which moves slowly, was shipped to 37 states from Maine to California and later was redistributed by wholesalers who cannot trace many of their sales. Some going back as far as 1946 have been found on the market. These ampuls may be in the hands of doctors, hospitals, clinics, and retail and wholesale druggists.

WOMAN'S AUXILIARY

The Woman's Auxiliary to the Louisiana State Medical Society has received this notice from the National Auxiliary Treasurer, our own Mrs. A. A. Herold, Shreveport. "The post-Convention meeting of the Board of Directors was held on June 24th, 1948. At this meeting the Board suggested I write to you and attempt to clarify for you some of the action taken at the Convention by the House of Delegates.

You perhaps recall that on June 23rd, the Convention adopted the following revision to the Constitution and By-Laws: Chapter VII. constituent Auxiliaries, Section 4, now reads—"Each constituent Auxiliary shall transmit to the Treasurer of this Auxiliary not later than March 15th annually dues amounting to one dollar for each of its members for the current year, which shall include subscription to the periodicals published by this Auxiliary, when authorized by the Advisory Council to the Woman's Auxiliary. This means in other words, that until the American Medical Association publishes the new periodicals and receives from the advertisements in the new publication enough funds to finance both this new publication and our Bulletin, we continue to pay a dollar for dues and another dollar for a year's subscription to the Bulletin.

For the present, the dollar sent to the State Treasurer for National dues does not include any subscription to any publication. This revision also became effective immediately upon its adoption, therefore, any dues paid prior to June 23rd should have been twenty-five cents, but any dues paid since that date must be one dollar. I hope this

explanation has helped you a little to understand the situation as it now stands regarding dues and publications."

This, of course, means that of the one dollar and a half collected now for State and National dues from each member of the Louisiana Auxiliary, one dollar will go to National and fifty cents will go to the State. The one dollar will be collected for the Bulletin as usual until further notice. Read your Convention issue of the Bulletin for further information. Continue to read the Organization section of this Journal and the A.M.A. Journal as well as the Bulletin, Hygeia and our own quarterly. The first copy of "News and Views" should be in your hands now. A vote of thanks should go to your President, Mrs. O. B. Owens and her assistants and also to Dr. A. V. Friedrichs, Dr. P. T. Talbot and the entire Council on Medical Service and Public Relations.

MRS. F. U. DARBY,
Press & Publicity Chairman.

BOOK REVIEWS

Physiology of Exercise: By Laurence E. Morehouse, Ph. D. and Augustus T. Miller, Jr., Ph. D., St. Louis, The C. V. Mosby Company, 1948. Pp. 353. Price, $4.75.

This is a small monograph embodying much of the work from the Harvard Fatigue Laboratory which was done before and during the war. It contains reviews of the physiology of muscle, circulation and respiration as introductions to the specific effects of exercise on the system. There are also brief chapters on skill, endurance, fatigue, physical fitness, training and diet.

It is questionable whether this monograph will be of any real value to the physician or to the advanced student interested in the subject of exercise. It will appeal more particularly to the more elementary student in physiology or physical education for whom it was obviously written. For the latter it should provide an excellent text. Perhaps the most valuable part of the book is the extensive bibliography added to each chapter. This bibliography contains review articles dealing with various aspects of the problem and is reasonably up to date, although it would seem that some of the more recent work done during the war might have been included.

H. S. MAYERSON, Ph. D.

Essays in Historical Medicine: By Bernard J. Ficarra, A. B., Sc. B., M. D. New York, Froben Press, 1948. Pp. 220. Price, $5.00.

This small volume contains eight essays, four of which have been reprinted from the periodicals in which they originally appeared. The subjects treated are: American Pioneers in Abdominal Surgery, Amputations and Prostheses through the Centuries, Famous Cripples of the Past, Surgical References in Shakespeare, Evolution of Blood Transfusion, Walter Reed at Kings County Hospital, An Historical View of Pathology and Famous Autopsies in History. The last-named essay includes descriptions of the autopsies on our three martyred Presidents.

The typography and general physical make-up of the book are good. It is unfortunate that some of the numerous illustrations are poorly reproduced. This title is a welcome addition to the historical section of the doctor's private library.

MARY LOUISE MARSHALL

The Oculorotary Muscles: By Richard G. Scobee, M. D. St. Louis, C. V. Mosby Company, 1947. Pp. 359. Price, $8.00.

The author has presented the subject from the standpoint of the clinician and in an orthodox manner. This book of some three hundred and fifty pages is the evolution of a series of lectures which the author has given numerous times, and represents a thorough understanding of the principles involved in the examination and care of patients with neuromuscular ocular disease. Although it does not present the technical advances which have been described by other recent authors on this subject, it will give the average reader a better understanding of the complexities encountered. The author has, to an exceptional degree, the ability to simplify complex and difficult concepts, and to adapt them in a practical manner for use by the average ophthalmologist. The use of specific questions and answers facilitates usability, as well as readability. The table of contents is especially well organized. The illustrations are numerous and well chosen. The alphabetic index is of moderate length and fairly comprehensive. Especially the younger ophthalmologist will make no mistake in reading and re-reading this excellent work.

CHAS. A. BAHN, M. D.

PUBLICATIONS RECEIVED

Blakiston Company, Philadelphia: Medical Writing (2nd edition), by Morris Fishbein, M. D.; Re-

cent Advances in Obstetrics and Gynaecology (7th edition), by Aleck W. Bourne, M. A., M. B., B. Ch. (Camb.), F. R. C. S. (Eng.), F. R. C. O. G. and Leslie H. Williams, M. D., M. S. (Lond.), F. R. C. S. (Eng.), F. R. C. O. G.

C. V. Mosby Company, St. Louis: Preoperative and Postoperative Care of Surgical Patients, by Hugh C. Ilgenfritz, A. B., M. D., F. A. C. S.

W. B. Saunders Company, Philadelphia: General Endocrinology, by C. Donnell Turner, Ph. D.

The Williams & Wilkins Company, Baltimore: Human Nutrition, by V. H. Mottram, M. A. (Cant.); Manual of Leprosy, by Ernest Muir, C. M. G., C. I. E., M. D., F. R. C. S. Edin.